THE UNIVERSITY OF CHICAGO

ANNUAL REPORT
2002-2003

CANCER RESEARCH CENTER
HOSPITALS & HEALTH SYSTEM CANCER PROGRAM
CANCER RESEARCH FOUNDATION

ANNUAL REPORT 2002-2003
William Rainey Harper, our first president said, "Ours is an institution whose aim it shall be to push forward the boundaries of medicine..." Dr. Frank Billings, the first chairman of Medicine in 1905 epitomized that aim by being the first clinician to describe the natural history of myocardial infarctions. Subsequent generations of scholars have remained true to that aim. The University of Chicago Hospitals have again been ranked in the top 15 hospitals in the U.S. News and World Report Honor Roll of the "best hospitals". The Cancer Research Center and its legacy of discovery dating back to the 1930's is integral to that global recognition. In the field of "cancer", the University ranks sixth among the top fifty cancer programs in the country. These achievements are not surprising in view of our long term commitment to cancer research. That commitment is realized by nurturing and recruiting the best possible talent and providing them with exceptional facilities.

Whether in the areas of faculty recruitment and retention, basic, population or clinical research, patient care or education our goal remains the same, the pursuit of excellence to improve all our lives. Achieving excellence in any field and maintaining that excellence is not easily accomplished. At the University of Chicago Cancer Research Center we believe that our successes depend on the strength of our team; cancer investigators supported by staff, such as laboratory technicians, nurses, data managers, pharmacists and many others. Since our last grant period we have worked hard to recruit the best and brightest cancer investigators to the UCCRC. Twenty-five new members have joined our ranks for a total of 175 Cancer Research Center members representing sixteen diverse departments at the University.

These cancer investigators interact through six dynamic cancer programs which continue to evolve; Cell Signaling and Gene Regulation, Molecular Genetics and Hematopoiesis, Immunology and Cancer, Clinical and Experimental Therapeutics, Advanced Imaging and Clinical Cancer Genetics and Prevention. Ongoing collaborations across these interdisciplinary programs are constantly encouraged to spark further breakthrough discoveries.

Illustrative of this effort is the awarding of a Health Disparities Grant from the National Cancer Institute to a group of breast cancer researchers, Dr. Sarah Gehlert from the School of Social Service Administration, Dr. Martha McClintock in the Department of Psychology and Drs. Funmi Olopade and Suzanne Conzen from the Department of Medicine, Section of Hematology/Oncology, who are investigating health disparities in breast cancer. This award is important as it recognizes our strength in breast cancer, our commitment to population science, particularly to underserved populations on the south side of Chicago, and the collaborative vision required to conduct interdisciplinary research.

Other notable achievements have been the continued creation of new scientific knowledge by our members. Innovative science is recognized by the awarding of peer-reviewed grants from the National Institutes of Health (NIH) and other institutions. This year, Drs. Albert Bendelac, Michelle LeBeau, Hans Schreiber and Julian Solway received Program Project Grants from the NIH. Program Projects Grants are extremely difficult to obtain and each of these principal investigators deserves accolades for these awards. Many other members have successfully obtained NIH funding among them; Dr. Bernard Roizman received an extremely prestigious NIH Merit Award; Dr. Mark Ratain, a NIH Cooperative Award to continue his internationally recognized work in new drug development and an additional 21 R01's were successfully recompeted or newly awarded in the last six months of fiscal year 2002-2003. One of the largest grants in the University’s portfolio is held by Dr. Rich Schilsky for his leadership since 1995 of the Cancer and Leukemia Group B (CALGB), one of the premier cancer clinical trial networks in the world.
Making innovative research facilities available to our researchers remains a top priority. The Interdivisional Research Building, under construction for completion in 2005, is designed to enhance collaboration and to ease the sharing of ideas among researchers. Plans are underway to link efforts in Biological Sciences with those in Physical and Social Sciences and with computational strength at Argonne National Labs which should facilitate future discovery. Further commitments have been made to establish additional research space in the Biological Sciences Division.

While challenges in the field of cancer research abound, UCCRC continues to overcome them and to produce exciting and novel data, with the help of our generous supporters. This year’s report provides a more comprehensive understanding of the cancer program at The University of Chicago with the inclusion of the Scientific Report of the Cancer Research Center, the Hospitals Cancer Program Annual Report and The Annual Report of The University of Chicago Cancer Research Foundation (UCCRF). We hope you will enjoy learning more about the ways your philanthropy makes new discoveries possible.

To each and every one of you, I say thank you for your help; thank you for your inspiration; thank you for believing with us that together we can make cancer a thing of the past!

Warmest regards,

Nicholas J. Vogelzang, M.D.
Fred C. Buffett Professor of Medicine
Director, the University of Chicago Cancer Research Center
CHAIRMAN’S MESSAGE

It is my privilege to present to you the 2003 Cancer Program Annual Report of the University of Chicago Hospitals. During 2002, the Cancer Registry abstracted over 2,300 new cases. Over seventeen hundred of these cases were analytic, with the greatest representation by tumors of the digestive tract, breast, respiratory and male genital organs. Follow-up on the analytic cases has consistently been greater than 90%.

This Annual Report includes highlights from all disciplines involved directly and indirectly with cancer patients, including physicians, nursing, quality improvement, cancer registry, and patient support services, and is reflective of the outstanding care given to our cancer patients at the University of Chicago Hospitals. Once again, the University of Chicago Hospitals was judged as one of the top ten cancer hospitals in the United States by U.S. News World Report. A special section is devoted to the diagnosis, staging and treatment of lung cancer.

This message would not be complete without thanking the members of the Cancer Committee and the Cancer Registry staff for their help throughout the year and for their contribution to this Annual Report. A special thank you to Jennifer Sepiol, our Cancer Registry Manager, who continues to energize the Cancer Registry and make changes that will be instrumental in positioning the registry for continued success in the future.

Sincerely,

Mitchell Posner, M.D.
Professor Department of Surgery, Section of General Surgery
LETTER FROM THE PRESIDENT OF
THE UNIVERSITY OF CHICAGO
CANCER RESEARCH FOUNDATION

I am pleased that the Cancer Research Foundation is a part of this year’s Annual Report in its new format. I hope you will find that the new design provides you with a more comprehensive understanding of the cancer program at The University of Chicago with the inclusion of the Scientific Report of the Cancer Research Center and the Hospitals Cancer Program Annual Report along with our account of the activities of The University of Chicago Cancer Research Foundation (UCCRF).

This year, as in the past sixty years, the UCCRF has continued its dynamic efforts to advance the cancer program at The University of Chicago with the same verve and determination of its founders, Maurice Goldblatt and the Goldblatt family. Our generous donors, auxiliaries and affiliates continue to raise financial support to advance breakthroughs in the fields of breast cancer, immunology, new anti-cancer drug development, cancer genetics, leukemia, advanced imaging and population science among others.

This support has helped to meet the ever-growing needs of The University of Chicago Cancer Research Center, one of the country’s premier institutions for the research, diagnosis, and treatment of cancer and home to a nationally and internationally distinguished medical staff and research team led by Dr. Nicholas J. Vogelzang.

In 2002, the boards of the Foundation continued to build on their successes. Our trustees, the Women’s Board, the Auxiliary Board and the Associates Board set priorities in the areas of board development and fundraising. We welcome our new board members and congratulate all our members on exceeding their philanthropic goals. How fortunate we are to partner with individuals truly devoted to the cause of cancer research!

Every gift takes us further in our quest to support existing cancer programs and those which must and can be developed in the future. Your participation in this process is vital. On behalf of our valued researchers and clinicians, let me express our greatest appreciation for your commitment and continued support of the UCCRF. Thank you all for your help in making cancer a thing of the past!

Sincerely,

Ruth Ann Gillis McGuinnis
President

EVERY GIFT TAKES US FURTHER IN OUR
QUEST TO SUPPORT EXISTING CANCER
PROGRAMS AND THOSE WHICH MUST
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PROGRAM 1:

MOLECULAR BIOLOGY OF CELL GROWTH AND DIFFERENTIATION
PROGRAM DIRECTOR: ANNING LIN, PH.D.

34 MEMBERS

The program on Molecular Biology of Cell Growth and Differentiation is multifaceted and is aimed at elucidating (i) molecular mechanisms underlying the balance of growth and differentiation in eukaryotic cells and (ii) how these processes go astray during cellular transformation leading to cancer. Particular strengths of the program include analysis of cell cycle control and apoptosis, signaling and transcriptional regulatory pathways in cellular differentiation and structural biology.

RESEARCH HIGHLIGHTS

Wei Du’s laboratory has examined the role of the hedgehog-signaling pathway in tumor formation using Drosophila as a model system. They report that hedgehog signaling promotes transcription of cyclin E and cyclin D, two inhibitors of RB. The discovery of a direct connection between Hh signaling and key cell cycle regulators provides insight into the mechanism by which Hh signaling can promote tumor formation.

Guido Franzoso’s laboratory has provided novel insight into the mechanism by which NFkB/Rel factors regulate cell survival. The anti-apoptotic activity of NFkB is crucial to oncogenesis and to chemo- and radio-resistance in cancer. They have shown that NFkB induces the gadd 45 β gene which in turn down regulates pro-apoptotic JNK signaling. These findings define a novel protective mechanism mediated by NFkB.

Dr. Marcus Peter’s laboratory has explored the role of the death effector domain containing DNA binding protein (DEDD) in apoptosis. Their data suggest that DEDD represents a novel scaffold protein that directs the effector caspase-3 to certain substrates thereby facilitating their ordered degradation during apoptosis.

Dr. Stephen Kron’s laboratory has implicated the cyclin-dependent kinase Cdc28 in yeast in maintaining genomic integrity during mitosis. They isolated temperature sensitive mutations in Cdc28 gene that inappropriately continue mitosis when the mitotic spindle is disrupted. High copy suppression of this mutant phenotype implicates the kinase Cak1 along with Cdc28 in an essential surveillance function required to maintain genetic stability through mitosis.

Dr. Wei-Jen Tang’s laboratory has solved the atomic structure of oedema factor, a calmodulin-activated adenylyl cyclase, which is important in the pathogenesis of anthrax. Dr. Geoffrey Greene’s laboratory has also used x-ray crystallography to analyze the mechanism by which the estrogen receptor antagonist THC exerts its effect. They provide evidence for a novel mechanism termed “passive antagonism.”

Dr. Harinder Singh’s laboratory has elucidated new functions of the ets family transcription factor PU.1 in regulating the growth and differentiation of myeloid as well as lymphoid cells of the hematopoietic system. PU.1 has been shown to directly control the transcription of myeloid and lymphoid cytokine receptor systems including G-CSFR, M-CSFR, and IL-7Ra. Furthermore, the Singh laboratory has established that PU.1 can function either antagonistically or cooperatively with the transcription factor GATA-2 to regulate alternate myeloid cell fates. These results have important implications for the mechanisms regulating cell fate choice in stem cells and multipotential progenitors.

In summary, the Molecular Biology Program at the UCCC continues to make major contributions to the understanding of cell growth, apoptosis and differentiation and how these processes are deregulated in cancer. Shared research interests, joint group meetings, journal clubs and seminar series foster an interactive and collaborative atmosphere. In the past six months, a very large number of new Investigators have applied to join the program. Discussions have been initiated within the Executive Committee to divide the program into two components – Molecular Oncology and Structure based Cancer Biology, so as to maintain programmatic coherence.
MAKING CANCER A THING

PROGRAM 2:
CANCER MOLECULAR GENETICS
PROGRAM DIRECTOR: MICHELLE M. LE BEAU, PH.D.
34 MEMBERS

OVERVIEW AND SCIENTIFIC THRUST

Molecular analysis of human tumors has led to the identification of a number of genes that are involved in the pathogenesis or progression of human tumors. Mutations in cancer-related genes result in the activation of dominant oncogenes or in loss of function of tumor suppressor genes, thereby leading to abnormal cell growth and differentiation. The overall objectives of the Cancer Molecular Genetics Program are (1) to integrate and focus the work of investigators with established research programs, (2) to characterize the biological and clinical features associated with specific genetic changes in the hematologic malignant diseases and solid tumors, and (3) to identify the genes that are involved in the pathogenesis or progression of human tumors as a result of recurring chromosomal abnormalities or other mutations. The program serves as a core of investigators with expertise in clinical cancer research, cancer cytogenetics, and molecular biology.

The program has a major focus on translational research. For example, the identification of recurring chromosomal abnormalities in human tumors and the correlation of these abnormalities with clinical features, a long-standing interest of this program, has led to the routine application of cytogenetic studies to hematologic malignant diseases and some solid tumors for diagnosis and sub-classification of the disease, and for the identification of prognostic factors. The investigators in the program are active in evaluating new therapies, including molecularly-targeted therapies. Other active areas of investigation include correlating genetic changes with clinical features in breast cancer, gliomas, prostate cancer, and bladder cancer, with the goal of improving the diagnosis and treatment of these diseases. Finally, program members have been very active in developing and testing new diagnostic procedures for the detection of genetic changes in tumor cells.

RESEARCH HIGHLIGHTS

Program investigators reported on the clinical, morphological, and cytogenetic features of 306 patients with therapy-related myelodysplastic syndrome or acute myeloid leukemia, representing the largest series to date.

Dr. Larson reported the results of the IRIS (International Randomized IFN vs. STI571/Gleevec) Study Group, the first clinical trial in newly-diagnosed chronic myelogenous leukemia, at the plenary session of the American Society of Hematology Annual Meeting. Gleevec/Imatinib proved to be superior to IFN plus cytosine arabinoside in terms of complete hematologic response, major cytogenetic response, complete cytogenetic response, and progression-free survival.

Drs. Le Beau and Crispino reported that somatic truncating mutations in the 5' region of the GATA1 transcription factor gene occur in all cases of acute megakaryoblastic leukemia in Down syndrome, suggesting that loss of full-length GATA1 contributes to the initiation or progression of the disease. This observation represents the first genetic mutation identified in this subtype of leukemia.

Dr. Stock demonstrated that quantitative real-time PCR of leukemia clone-specific rearrangements of IGH or TCR genes is a sensitive method to detect minimal residual disease in adult acute lymphoblastic leukemia, and is a novel prognostic marker.
Dr. Thirman identified ELL, a MLL-fusion partner in acute myeloid leukemia, as a component of Cajal bodies, linking the transcriptional elongation activity of ELL to the RNA processing functions of Cajal bodies. In leukemia cells with the fusion, MLL-ELL is delocalized from the Cajal bodies, indicating that disruption of ELL function may play a role in leukemogenesis.

Dr. Baron identified a pro-apoptotic gene, human programmed cell death-2 (PDCD2) as a target of transcriptional repression by BCL6 in lymphomas.

Dr. Olopade determined that the BRCA2 T2722R missense mutation identified in familial breast cancer disrupts a functional exon splicing enhancer resulting in exon skipping. This represents the first BRCA2 missense mutation shown to be a deleterious protein-truncating mutation.

Dr. He identified deregulation of β-catenin signaling in a high proportion of human osteosarcomas.

Dr. Rinker-Schaeffer demonstrated that MKK4 is a metastasis suppressor gene in ovarian carcinoma.

Dr. Le Beau characterized the cytogenetic pattern of leukemias in mouse models for acute promyelocytic leukemia (APL) expressing PML-PARA alone or the fusion plus cooperating mutations. The resultant leukemias have a defined spectrum of genetic changes that recapitulate the cytogenetic abnormalities found in human APL. The particular combination of initial cooperating events determines the leukemogenic pathway and the type of additional changes needed to complete malignant transformation.

Drs. Le Beau and Larson defined distinct subtypes of therapy-related leukemia using gene expression profiling.

Drs. Rowley and Wang defined the gene expression pattern of CD34+ hematopoietic stem/progenitor cells, and cytogenetic subsets of AML, including leukemias with the t(15;17), t(8;21), t(9;11), and inv(16).

**TRANSLATIONAL ACCOMPLISHMENTS**

The program has a major focus on translational research and, thus, contributes to the preeminent goal of the UCCRC. For example, the identification of recurring chromosomal abnormalities in human tumors and the correlation with clinical features, a long-standing interest of this program, has led to the routine application of cytogenetic and molecular studies to hematologic malignant disease, as well as some solid tumors, for diagnosis and subclassification of the disease and for the identification of prognostic factors. The investigators in the program are also active in correlating genetic changes with clinical features in breast, endometrial, ovarian, prostate cancer, osteosarcoma and significant correlations have already been identified. These initial studies can now be extended to prospective analyses of cancer patients with the goal of improving the diagnosis and treatment of malignant diseases.

Many of the ongoing projects described above illustrate the translational nature of the Program. For example, the IRIS study chaired by Dr. Larson, evaluating Gleevec/Imatinib vs. IFN plus AraC, demonstrated that Imatinib was superior to IFN plus AraC for first-line therapy for CML. Dr. Stock's demonstration that minimal residual disease detection using quantitative real-time PCR of IGH/TCR rearrangements is a novel prognostic marker in adult ALL may allow clinicians to alter or intensify treatment in first complete remission. Dr. Olopade's demonstration that a BRCA2 missense mutation results in disruption of exon splicing, and of a deleterious protein-truncating mutation suggests a novel approach for determining the clinical significance of a subset of the many unclassified variants in BRCA1/BRCA2, which is essential for accurate risk assessment. Dr. He recently determined that the β-catenin signaling pathway is deregulated in osteosarcomas, a poorly characterized tumor type. Using this information, he has initiated a high throughput screen for candidate anti-cancer agents that specifically inhibit β-catenin signaling. A final example of research with translational implications is the collaboration between Drs. Le Beau and Larson to define the gene expression profile of t-AML, and the identification of distinct subgroups. Establishing the molecular pathways involved in t-AML may facilitate the identification of selectively expressed genes that can be exploited for the development of urgently needed targeted therapies.
PROGRAM 3:

IMMUNOLOGY AND CANCER
PROGRAM DIRECTOR: THOMAS F. GAJEWSKI, M.D., PH.D.

24 MEMBERS

OVERVIEW

The overall goals of the Immunology and Cancer Program are to understand the interface between the host immune system and a malignant tumor, and ultimately to manipulate that interaction to promote immune-mediated tumor destruction in patients with cancer. The research activities thus span fundamental investigations in immunology, mouse models of anti-tumor immunity, and novel immunotherapy clinical trials. Observations made in early clinical studies have generated new hypotheses that are being addressed back in murine models. The Immunology and Cancer Program has thus evolved into an important example of bi-directional translational research, with ideas moving freely between bench and bedside. The continued success of our program is evident in the publication of more than 106 papers, including many in the highest caliber journals.

Although much of the immunotherapy field has moved forward quickly on the development of cancer vaccine strategies, it may be important to take a step back and analyze the failure of the immune system to spontaneously reject most cancers from a more global perspective. It is thought that essentially all cancers express antigens that have the potential to be recognized by the immune system as foreign. Certainly, in some instances the failure to reject antigenic tumors may be secondary to failed generation of a tumor-specific T cell response. However, additional mechanisms of immune escape lie downstream from initial T cell priming, as it is important for activated T cells to differentiate appropriately into effector cells, expand to sufficient numbers, survive in the periphery, traffic to tumor sites, continue to function and survive in the tumor microenvironment, and directly contact tumor cells. In addition, the tumor cells themselves must continue to express antigen, the antigen processing machinery, and MHC molecules for optimal recognition. Finally, although much of the field focuses on T cell responses, the role of innate immunity remains under-emphasized. Thus, in addition to optimizing cancer vaccine approaches, understanding all aspects of the immune response against tumors will be vital for clinical success. These insights will be guided by continued study of fundamental aspects of immune regulation, and thus a great degree of our effort lies in such basic immunologic studies.

The research focus of our members spans from the molecular biology of gene regulation and development, to the biochemistry of signal transduction, to the mechanisms of immune responses and tolerance in vivo. The Immunology and Cancer Program maintains an environment that promotes collaboration among its members, catalyzes a cancer focus, and promotes translation to the clinic.

RESEARCH HIGHLIGHTS

Somatic Mutation Mechanisms

Somatic mutation is firmly established as a molecular cause of many types of cancer, and leads to the generation of neoantigens. Therefore, the studies of Drs. Ursula Storb and Terrence Martin on the mechanisms of this process are uniquely important for the understanding cancer biology. They are studying the somatic hyper-mutation of Ig genes which they had shown previously is dependent on the initiation of transcription. They have recently identified a cis element in Ig genes that is an enhancer of mutation without being an enhancer of transcription. They have observed that the known transcription factor, SpiB, is involved in the selection in germinal centers of B cells with beneficial mutations, but SpiB is not required for the basic mutation process. They also have found that the high fidelity polymerase delta is not likely to be made into an error prone polymerase during somatic mutation. Finally, they have observed that somatic mutation and switch recombination are intimately linked during the expansion of a B cell clone. Drs. Storb and Martin will continue to work toward identification of the molecular mechanisms of somatic hyper-mutation.
Transcriptional Regulation of Hematopoietic Development

Hematopoietic cells and cells of the vascular network differentiate in developing blood islands. Understanding the regulation of hematopoietic development and blood vessel formation is critical to gain insights into tumor-stromal interactions. There is growing evidence that cell type-specific transcription factors play a critical role in the development of these cell lineages, and therefore a major focus is on the transcriptional regulation of this process. Dr. Harinder Singh’s laboratory has been defining the functions of the transcription factor PU.1 in the development of immune cells. They have observed that PU.1 is required for expression of the IL-7 receptor and thus dictates the development of lymphoid progenitors. They also have collaborated to determine the crystal structure of the PU.1/IRF-4/DNA ternary complex, leading to a better molecular understanding of the transcriptional regulation by this molecule.

T Cell Development

As T cells are central to adaptive immune responses to tumor antigens, a greater understanding of T cell development and central tolerance will provide important insights into the shaping of the repertoire that includes precursors specific for tumor antigens. Dr. Thomas Gajewski’s laboratory has investigated the role of the putative negative regulatory receptor PD-1 on T cell development. Using 2C TCRTg/RAG2-/-/PD-1-/- mice, they have observed that absence of PD-1 alters thymic selection. These results are consistent with PD-1 negatively regulating the threshold of TCR signaling in T-lineage cells, and have implications for the development of autoimmunity and anti-tumor responses.

Two members of the program are studying the development of NKT cells. Dr. Albert Bendelac’s group has elucidated several new thymic developmental steps that control the generation of CD1d-autoreactive NKT cells, a cell-type that regulates the immunological rejection of many tumors. They also have begun to unravel, at the genetic level, a proteolytic cascade leading to the generation of glycolipid ligands for NKT cells. Dr. Chyung-Ru Wang’s lab has shown for the first time that NKT cells are susceptible to negative selection when engaged by high-avidity glycolipid antigen or abundant self antigen. In addition, they have found that NKT cells escape negative selection primarily by altering TCR usage and decreasing affinity to CD1d and its ligand. Many characteristics distinguish the differentiation of NKT cells from conventional T cells in adult mice, including the cell type responsible for their positive selection. Their study, however, demonstrates that, like conventional T lymphocytes, the negative selection of NKT cells is enhanced when overall avidity is increased, and is mediated by CD1d-expressing dendritic cells.

Inflammation and Innate Immunity

Chronic tissue inflammation has been shown to favor the development of certain cancers, such as MALT lymphomas. Inflammation and activation of innate immune cells also comprise the first step toward the development of an adaptive immune response, and thus a better understanding of this process may instruct how tumors evade immune destruction and how to better overcome this evasion. Several members of the Program investigate aspects of mucosal inflammation. Dr. Martin’s laboratory is continuing work on the novel growth factor AMP-18, which is specifically expressed at high levels in the gastric antrum. Certain peptide fragments of the AMP-18 protein have mitogenic and motogenic properties, while others can inhibit the activity of the AMP-18 protein. They propose that this novel growth factor is important in the maintenance and repair of the gastric epithelium. Dr. Barbara Henderickson’s laboratory is investigating the role of adherent gram-negative bacteria in promoting carcinogenesis of the colon. They have found that increased numbers of mucosa-associated aerobic gram-negative bacteria – particularly E. coli – are associated with certain pathologic conditions of the colon including colonic adenomas. Moreover, they have identified patient-derived E. coli isolates that are capable of altering the biology of intestinal epithelial cells in vitro. Dr. Yang-Xiu Fu’s laboratory has discovered a novel mechanism of IgA transport across the lamina propria.
Dr. Averil Ma’s laboratory has been investigating the role of the A20 protein in tissue inflammation. They have generated A20-deficient mice and have found that they develop profound autoimmunity coupled with an inability of cells to terminase TNF-induced NF-kB responses. A20-deficient cells are surprisingly also more susceptible to TNF-induced apoptosis. Ongoing studies are focusing on the biochemical mechanism by which A20 terminates NF-kB and JNK signaling. The implications of these studies extend beyond the regulation of inflammation, as both NF-kB and JNK signaling pathways are proto-oncogenic in several cell types.

Dr. Bana Jabri is investigating the mechanism of NK cell regulation by the receptors CD94 and 2B4, which are of particular interest because they are also expressed in T cells in which they serve a distinct biochemical function.

Dr.Vinay Kumar continues his study of activating and inhibitory receptors on NK cell function. They have observed that the activating receptor 2B4 is also expressed on activated T cells, in which it is associated with LAT in GEMs. The differences between NK receptor function on T cells versus NK cells remains an active area of investigation.

Dr. Raymond Roos is continuing his studies of the pathogenesis of Theiler’s virus, which causes a chronic demyelinating disease and persistent infection. Their recent studies have demonstrated the importance of host proteins that bind the viral RNA genome and are important in regulating the efficiency of virus RNA translation. These proteins are cell type-specific, and thereby can play an important role in determining the neurovirulence of the virus. They have identified an alternatively translated Theiler’s virus protein that is critical for virus persistence and demyelination. Recent results suggest that this viral protein affects CD4+ T cell function, and thereby interferes with virus clearance.

**Tumor Antigen Presentation**

Activation of T cells against tumor antigens begins with successful processing and presentation of antigenic peptides by antigen-presenting cells. Several research projects are analyzing the nature of antigens, the mechanisms of presentation in vivo, and the recognition of these antigens by the TCR.

Dr. Schreiber’s laboratory has dissected the pathways for tumor antigen presentation in vivo. They have observed that tumors expressing high levels of antigen are effectively cross-presented by host APCs in vivo, but that tumors expressing low levels of antigen that can only present antigen directly grow progressively due to a stromal cell “barrier”. Dr. Schreiber’s laboratory also continues to study the nature of tumor antigens generated by point mutation, in particular those derived from ribosomal proteins.

Dr. Fu’s laboratory has observed that anti-tumor T cell activation and tumor rejection can occur in the absence of host lymph nodes or spleen, arguing that cross-priming via host APCs does not absolutely require these secondary lymphoid organs.

**Lymphocyte Signal Transduction**

Lymphocytes respond to the presence of antigen by signal transduction through the antigen receptor. The T cell receptor (TCR) and B cell receptor (BCR) are thus the central mechanism by which the adaptive immune system recognizes the presence of tumor antigens. Understanding the details of this process is of central importance to the Program.

Dr. Gajewski has continued his study of Ras function in T cell anergy. Using a novel coxsackie/adenovirus receptor transgenic mouse and an adenoaviral vector encoding active Ras, he has shown that active Ras restores IL-2 production in anergic T cells. To determine the mechanism of Ras hypofunction in T cell anergy, a gene array screen was performed. This revealed overexpression of an attractive candidate, DAG kinase. In fact, an inhibitor of DAG kinase restored IL-2 production in anergic cells, arguing that increased DAG kinase activity and decreased Ras activation play a major role in the anergic state.

Dr. Alegre’s group has examined the signaling properties of the TNF receptor family member CD30. They have found that CD30 engagement can affect T cell function independently of TCR stimulation. Indeed, ligation of CD30 on previously activated cells was found to induce IL-13 production in the complete absence of TCR stimulation. This effect was dependent on the presence of TRAF2, a molecule that is known to bind to the cytoplasmic tail of CD30, and on intracellular activation of p38, but not that of NF-kB. Dr. Alegre has also continued to study the functional properties of the inhibitory receptor CTLA-4. They have found that CTLA-4 cross-linking results in reduced TCR-mediated NF-kB activation, and that lack of CTLA-4 results in markedly increased levels of activated NF-kB. To determine if elevated NF-kB activity in T cells was playing a role in the lymphoproliferation in CTLA-4-deficient mice, they intercrossed CTLA-4-deficient mice with mutant mice defective in NF-kB activation. The resulting mice have a much attenuated disease when compared with control CTLA-4-deficient animals, indicating that increased NF-kB activation in T cells is one of the mechanisms by which lack of CTLA-4 results in progressive lymph accumulation.
Polarity in T Cell Activation

A group of investigators in the program have been addressing the polarity that is inherent to the effector function of helper and cytotoxic T cells.

Drs. Sperling and Burkhardt have continued to study the regulation of the “antipole” in T cell activation. They found that when T cells contact antigen presenting cells, the receptor CD43 is actively removed from the contact area, when an actin binding protein, talin, is concentrated in the area.

Peripheral T Cell Differentiation

Naïve T cells that encounter antigen differentiate into effector cells that mediate functions such as cytolysis of tumor cell targets. Studies of T cell differentiation are thus critical to understanding T cell-mediated effector functions in vivo.

Dr. Gajewski’s laboratory has shifted a major focus toward the study of peripheral CD8+ T cell differentiation. Using a gene array screen to identify differentially expressed genes in naïve versus effector CD8+ T cells, they have found multiple attractive candidates for regulating the functional attributes of these 2 differentiation states. One category of upregulated genes is involved in glucose-dependent metabolism. Mechanistic studies have determined that glucose is particularly required for IFN-γ gene expression in effector CD8+ T cells, having implications for the role for metabolic restrictions characteristic of the tumor microenvironment on T cell effector function.

Dr. Sperling’s laboratory continues their studies of Th2 differentiation and allergic airway disease. They have observed that Fas regulates the survival of T cells that mediate airway inflammation, and that the costimulatory receptor ICOS is a critical regulator of Th2 differentiation in this model.

T Cell Memory

A central characteristic of adaptive immunity is the induction of memory. The generation of a stable, functional memory T cell population against tumor antigens is an ultimate goal in tumor immunology.

Drs. Ashton-Rickardt and Ma are continuing their work on the regulation of T cell memory. Dr. Ma’s group has collaborated to investigate the role of IL-15 in the activation and memory of CD8+ T cells. They have observed that IL-15 is required for long-term maintenance of memory cells and that in some cases it may contribute to CD8+ T cell expansion.

Dr. Yang-Xin Fu is studying the importance of lymphotoxin in the lymphoid microenvironment. They have recently observed that the deficient lymph node organization in lymphotoxin-deficient mice can be complemented by LIGHT, a newly discovered TNF family member. These results have implications for the trafficking and activation of T cells in secondary lymphoid organs in vivo.
Immune Tolerance and Autoimmunity

One mechanism by which tumors are allowed to grow despite expression of antigens is via the induction of peripheral tolerance. Uncovering the mechanisms of tolerance, and how tolerance fails in the case of autoimmunity, should illustrate strategies to reverse the process and facilitate anti-tumor immune responses.

Dr. Leslie DeGroot’s laboratory has identified an association with a specific allele of the CTLA-4 gene with Graves’ disease, a form of autoimmune thyroiditis. The CTLA-4 gene has three polymorphic forms with nucleotide variation in the promoter area, AG allelism in the first intron, and an AT polymorphic repeat in the 3’ untranslated region. The latter two polymorphisms are in close linkage, and the A polymorphism in the first exon and the long AT repeat are both linked with the occurrence of Graves’ disease. They have shown that lymphocytes bearing the associated forms of CTLA-4 produce less inhibition of T cell proliferation in response to antigen than do the alleles carrying the G nucleotide or the short form of the AT repeat. The basis of this effect remains under active investigation, and has implications for ongoing studies of anti-CTLA-4 mAb treatment as a cancer immunotherapy.

Dr. Richard Quigg’s group is investigating the immunopathogenesis of renal diseases. These include glomerular diseases, including membranous nephropathy, lupus nephritis and diabetic nephropathy; ischemia-reperfusion injury; and endotoxin-mediated acute renal failure. A long-standing interest in the role of the complement system guides some of his work. This year, Dr. Quigg has demonstrated that transgenic expression of a complement inhibitor increases survival of MRL/Lpr mice.

Dr. Fu has observed that administration of an anti-41BB mAb can prevent autoimmunity in Lpr mice. This effect appears to be mediated through increased survival of conventional CD8+ T cells that inhibit the accumulation of the abnormal autoreactive cells that occur in Lpr strains. This observation has important implications for the treatment of certain autoimmune syndromes, and suggests that anti-41BB costimulation-based therapy as a cancer treatment is not likely to pose an autoimmune risk.

Apoptosis

The final step of immune-mediated tumor cell killing involves apoptosis of successfully recognized target cells. Therefore, a detailed understanding of apoptotic death should illustrate potential mechanisms of resistance to immune destruction and uncover strategies to augment tumor elimination. Dr. Marcus Peter's laboratory has recently found that the death receptor Fas clusters and internalizes in a caspase-8- and F-actin-dependent fashion. They also found that this occurs only in so-called Fas Type I cells. Another apoptosis regulator being investigated is DEDD. They recently observed that DEDD is a quantitatively monoubiquitinated protein that regulates the activation of effector caspases such as caspase-3, thereby facilitating cleavage of intermediate filament proteins during apoptosis. Their data suggest the existence of a novel caspase activation complex that is independent of the classical apoptosome and that is regulated by DEDD. Work is ongoing to understand the implications of these observations for tumor growth and for T cell regulation in vitro and in vivo.

Mouse Models of Anti-tumor Immunity

Ultimately, concepts regarding interactions between a growing tumor and the host immune system must be examined in animal studies. Both fundamental immunology questions and preclinical therapeutic testing rely heavily on murine models of anti-tumor immunity.
Dr. Gajewski’s laboratory has investigated the role of the negative regulatory receptor PD-1 in impeding effective anti-tumor responses in vivo. They found that a ligand for PD-1, called PD-L1, is inducibly expressed on all murine and human tumor cells examined. Using PD-1−/− TCR transgenic T cells, they showed that absence of PD-1 augments tumor rejection in vivo. These results support the development of antagonists of this pathway to augment T cell-mediated tumor rejection in the clinic.

Drs. Alegre and Gajewski have investigated further the role for CTLA-4 in controlling anti-tumor T cell responses in vivo. They observed that mice deficient in CTLA-4 have markedly increased anti-tumor responses. Conversely, cross-linking CTLA-4 using membrane-bound anti-CTLA-4 antibody expressed on tumor cells resulted in a dramatic reduction in T cell responses in vitro and in vivo, thus promoting massive tumor growth. T cells from these animals had a phenotype consistent with anergy. Therefore, targeted ligation of CTLA-4 may be a therapy applicable to the treatment of autoimmune diseases or the prevention or treatment of acute allograft rejection, and CTLA-4 blockade should be pursued in tumor settings.

Dr. Bendelac’s laboratory has dissected the role of NKT cells in mediating the anti-tumor efficacy of IL-12 in vivo. They also are using this model to identify tumor-derived products that are recognized by NKT cells to promote tumor rejection.

Dr. DeGroot has continued his work on cytokine gene therapy for thyroid cancer. His laboratory has developed systems that allow expression of the genes encoding thymidine kinase, IL-2, or IL-12 in specific cancer types. Expression is targeted to differentiated thyroid cancer cells through the use of the thyroglobulin promoter, or to medullary thyroid cancer cells by use of the calcitonin promoter. This viral therapy works extremely well to induce tumor regression in model animal systems. They are currently developing improved vectors with the hope to translate this approach into therapy for human subjects with these cancer types in the near future.

Clinical Trials

The translational aspects of our Program are growing, a number of clinical trials have been recently completed, and new clinical studies are under development.

Dr. Gajewski’s group has completed a phase II study of immunization with Melan-A peptide-pulsed PBMC + rhIL-12 in patients with advanced melanoma. Of 20 patients treated, they observed that 2 patients had a complete response, 5 patients had a minor or mixed response, and 4 had stable disease. The median survival was better than expected, and immune responses measured by antigen-specific ELISpot were correlated with clinical outcome.

Drs. Harlin and Gajewski along with Dr. Vogelzang have examined immunologic parameters that correlate with clinical response following non-myeloablative allogeneic stem cell transplantation for renal cell carcinoma. They observed that clinical tumor regression was associated with expansion of CD8+ T cells and with IFN-γ production by CD8+ cells. These observations form a foundation for identifying tumor-specific T cells that mediate the graft-versus-tumor effect of this therapy.

New vaccine clinical trials have been initiated or are far along in development. A PSMA peptide vaccine + rhIL-12 for advanced prostate cancer has been initiated. A CEA vaccine for pancreatic cancer patients has been developed and will be initiated soon. In addition, a G250 peptide vaccine for renal cell carcinoma is being developed. The expansion of our portfolio of vaccine studies will be facilitated by the new cGMP facility.

Drs. Michael Nishimura and Mark McKee are pursuing an adoptive therapy strategy using T cell receptor (TCR) gene-modified lymphocytes for the recognition of tumor-associated antigens (TAA). In this strategy, TCR genes that confer tumor recognition to human T lymphocytes are identified and cloned. These genes are then transferred to peripheral blood lymphocytes (PBL) that have been harvested from a cancer patient, the transduced cells are activated and expanded in vitro, and the transduced cells are finally returned to the patient using adoptive therapy methodology. This type of gene transfer study has been successfully performed in a pre-clinical model using T cells that recognize the melanoma TAA MART-1. Dr. McKee is extending this work toward the identification of carcinoembryonic antigen (CEA)-specific human T cells and TCRs. It is anticipated that this strategy will be applied toward the clinic within the next 2 years, and will rely on the services of our new cGMP facility.
PROGRAMMATIC DEVELOPMENTS

Several changes have been made to increase the clinical translational aspect of the Program, to broaden its scope, to increase collaboration, and to augment its impact.

The Human Immunologic Monitoring (HIM) core facility is running full steam and has allowed us to increase our clinical trial efforts by enabling scientific immunologic questions to be asked in the context of immunotherapy clinical trials performed by existing oncology faculty. In addition, construction has been completed on our new cGMP facility, providing a state-of-the-art clinical grade cell processing laboratory for future clinical trial development. The Immunology Program will rely heavily on these resources as the clinical/translational activities continue to increase.

Finally, several initiatives have been made to increase the impact of the Program. Our monthly Immunology and Cancer conference has been expanded to include better representation of our basic science members. The purposes of these sessions are to facilitate collaboration, catalyze translation of new concepts toward clinical application, and to highlight clinical observations that deserve attention back in the laboratory. We have committed to sponsoring one speaker per year in our weekly Committee on Immunology seminar series on a topic of tumor immunology. This year we supported the visit of Andy Weinberg who discussed OX40 co-stimulation and anti-tumor immunity. Finally, we have recognized that our group is not as well-represented at national tumor immunology meetings as it could be, particularly with respect to our translational efforts. To this end, we have committed to providing travel grants for students and post-doctoral fellows to present abstracts at relevant meetings on tumor immunology topics. This year, 4 applications will be supported, 2 for the Keystone meeting on tumor immunology and 2 to the annual AACR meeting.

PROGRAM 4:

CLINICAL AND EXPERIMENTAL THERAPEUTICS

CO-PROGRAM LEADERS: EVERETT E. VOKES, M.D. AND M. EILEEN DOLAN, PH.D.

57 MEMBERS

OVERVIEW

During 2002, the Clinical and Experimental Therapeutics Program continued to be active on a broad scale.

The program has a long focus on drug development at all phases of clinical testing. Clinical trials enrollment included 1229 patients to 160 protocols in 2002; 254 patients were treated on phase II protocols and 204 patients on phase I studies (1/1/02 to 12/12/02). Clinical trials span the gamut from pre-clinical development to investigator-initiated phase I clinical trials to phase II trials in the regional phase II network to population pharmacology and pharmacogenetic studies. They incorporate correlative laboratory studies, including pharmacokinetic studies, genotyping studies, and measurement of surrogate endpoints. Clinical trials represent multidisciplinary teams, each comprised of a group of clinical investigators representing Medical Oncology, Radiation Oncology, Pathology and appropriate surgical specialties. Clinical efforts focus on studies of new drugs (cytotoxic or cytostatic) with clinical and translational endpoints, sequencing of multidisciplinary treatment, organ preservation, transplantation, and treatment intensification as strategies to increase cure rates and response. Imaging, surgical, and pathology support is available.

There are numerous multidisciplinary groups at the University of Chicago that meet on a weekly basis to review individual patient data, including history, physical, radiological studies, standard and investigational therapy options, and protocols. Phase I and II conferences are well attended by investigators, fellows, research scientists, research nurses and data managers. Discussion centers on patient toxicities, documented responses, evaluation of new therapies, correlative studies and treatment decisions.

In addition to weekly review of individual patient data, conferences held to increase awareness of novel therapies include a clinically oriented conference held weekly and a research-based conference held three times per month. Four times a year investigators from University of Chicago, Northwestern University, University of Illinois, and other major medical centers in the Chicago area meet to discuss pre-clinical and clinical research relating to investigational anti-cancer therapies or novel approaches to cancer treatment. These meetings stimulate collaborative research in the area of cancer treatment in the Chicago area.
CLINICAL DRUG DEVELOPMENT

Phase I program (selected protocols)


- A phase I escalates multiple dose study with continuous dosing of ABI-751 in patients with advanced cancer. (G. Fleming, P.I.)

- Randomized discontinuation study of BAY43-9006 in patients with advanced retractive cancer. (M. Ratain, P.I.)

Phase II program (selected protocols)

Currently, a total of 11 institutions are actively participating in the phase II network. In addition, we collaborate with other phase II contract holders for selective protocols of mutual interest. A total of 254 patients have been entered in calendar year 2002. A total of 12 protocols are actively accruing patients. Six protocols are under active development with NCI (5 protocols from other phase II contract holders are awaiting IRB approval), and 6 LOIs are currently under review. Eighteen LOIs were submitted over the last year. Eight were disapproved, four were approved, and six are still being reviewed.

- Phase II Study of ZD1839 (Iressa) in Recurrent or Metastatic Squamous Cell Carcinoma (SCC) of the Head and Neck (E. Cohen, F. Rosen, E. Vokes)

- SU5416 in Mesothelioma, Melanoma, Colon, and Prostate Cancer (Kindler HL, Vogelzang NJ, Stadler WM, TF Gajewski, GS Karczmar, R. Heimann)

- A phase II trial of bevacizumab (NSC#704865) plus gemcitabine in patients with advanced pancreatic cancer. (H.L. Kindler, L. Skoog, A. Brich, E. E. Vokes)

- Phase II study of Gleevec (Imatinib Mesylate formerly known as STI-571) in Patients with Myelofibrosis. (O.M. Odenike, R.A. Larson and W. Stock)

- Phase II study of a vaccine consisting of Melan-A peptide-pulsed PBMC + rhIL-12. (T. Gajewski)

PRECLINICAL DRUG DEVELOPMENT

Recent emphasis in the Clinical and Experimental Therapeutics Program has been on the development of studies of DNA repair modulators and understanding apoptosis.

- Role of DNA ligase IV/XRCC4 in carcinogenesis (K. Frank)
- Modulation of O6-Alkylguanine DNA alkyltransferase. (E. Dolan)
- Role of BRCA1 in DNA repair (D. Bishop)
PRECLINICAL PHARMACOGENETIC STUDIES

- UDP-glucuronosyltransferase 1A1 promoter (S. Das, M. Ratain)
- Human Carboxylesterase polymorphisms (E. Dolan, S. Das, M. Wu)

In conclusion, the Clinical and Experimental Therapeutics program of the UCCRC is vigorous and dynamic. It continues as one of our stellar programs.

PROGRAM 5:
ADVANCED IMAGING
PROGRAM LEADER: MARYELLEN L. GIGER, PH.D.

16 MEMBERS

OVERVIEW

Imaging is used in virtually every cancer patient, in many animal models of cancer, and in a large number of in vitro cancer-related experiments. Imaging research is thus fundamental to advanced cancer research. The Program in Advanced Imaging within the University of Chicago Cancer Research Center (UCCRC) is focused on enhancing the collaboration among imaging scientists involved in cancer research at the University of Chicago. Recent advances in image analysis methods as well as in computer processing speeds have led to and facilitated an expanded interest in research in quantitative image analysis. Image analysis investigations now underway within the UCCRC include work with x-ray images, ultrasound images, magnetic resonance images, radionuclide images, and molecular and physiological modeling. With the opening of a 14,000 square foot Imaging Research Institute in March 2000 and a new positron emission tomography (PET) devise within 15-18 months, imaging research within the UCCRC is continuing to expand.

The goals of the Advanced Imaging Program are (1) to foster cutting-edge imaging research in cancer diagnostics and treatment; (2) to translate laboratory imaging developments into clinical application; (3) to provide increased visibility and expansion of the strong base of imaging scientists in the UCCRC; (4) to further strengthen and broaden the training of predoctoral and postdoctoral students in the current graduate programs in Medical Physics; and (5) to enhance scientific interactions and collaborations among cancer researchers who investigate and develop imaging techniques for cancer detection and/or evaluation of treatment outcome.

The overall objective of the UCCRC Advanced Imaging Program is to integrate and focus the work of investigators with established research programs, to investigate new methods for the production and analysis of images for prevention, diagnosis, and treatment of cancer, and to translate developed methods from the laboratory to the clinical arena. The research objectives are:

1. To investigate new methods for computerized image analysis to help in the early diagnosis of cancers (breast, lung, colon, and prostate)
2. To investigate new methods of image reconstruction for use in CT (computed tomography), SPECT (single photon emission computed tomography), and PET imaging
3. To develop new methods of image acquisition such as MRIS (magnetic resonance imaging and spectroscopy) and EPR (electron paramagnetic resonance imaging) methods
4. To identify imaging methods for oncology practice and for the evaluation of response to target-based cancer drugs
5. To investigate methods for the evaluation of imaging systems, especially as they apply to computer-aided diagnosis
One of the major research themes in Advanced Imaging is computer-aided diagnosis (CAD), which involves computer vision and artificial intelligence techniques for mammography, chest, and colon imaging to ultimately aid in the earlier detection of cancer. In addition, radiopharmaceutical research is being performed in order to better understand blood flow, glucose metabolism and receptor pharmacology. EPR oxymetric imaging is being investigated to define aspects of tumor/tissue physiology in response to cytotoxins including radiation and chemotherapeutic agents. Research in magnetic resonance spectroscopy is being performed for the investigation and monitoring of angiogenesis. Investigators are also developing computer graphics for the creation of 3D, rotating, and shaded surface displays of organs and lesions in MRI images. Functional MRI is being investigated as a means to obtain functional as well as structural information from images. Researchers are also developing three dimensional treatment plans, dose calculations and graphic displays using CT, MRI, and PET images. Researchers from the various labs are collaborating in developing multimodality image correlation techniques to correlate multiple volumetric imaging studies of patients using images from CT, MRI, SPECT, and PET.

The highly interactive research conducted by the members of the Advanced Imaging Program benefits the UCCRC. The Program is strengthened by the contributions of a number of internationally recognized leaders in medical physics, medical imaging, radiology, and radiation oncology. Computers are playing an ever greater role in cancer detection and in the monitoring of treatment outcome. Technology transfer of techniques from other areas of imaging (such as national defense) is a reality. The Program in Advanced Imaging enhances the research of the investigators involved and gives them a better opportunity to further advance the field and continues to be an important resource for other UCCRC investigators. Moreover, the Program contributes to the training of younger scientists. The impact of advanced imaging on cancer research in the areas of screening, diagnosis, and treatment is clearly demonstrated by various projects in this Program. The potential impact on other areas, such as cellular imaging, exists to aid in the fundamental understanding of cancer progression.

Recent advances in image analysis methods as well as in computer processing speeds have increased the amount of research in quantitative image analysis. In addition, imaging methods can help in other cancer research programs by improving the visualization and analysis of data.

The Advanced Imaging Program benefits greatly from the interaction between members of the program and between other programs and investigators within the UCCRC. The UCCRC provides opportunities for collaborative research that bridge the laboratory developments and clinical applications, but which also bridge departments and other academic structures. For example, Drs. Giger, Nishikawa, and Jiang (medical physicists) are collaborating with Drs. Newstand and Schmidt (mammographers) in the clinical validation and translation of computer-aided diagnosis for the early detection of breast cancer. Similar collaborations between Drs. Armato, Giger, and Doi (medical physicists) and Dr. MacMahon (clinical chest radiologist), and between Drs. Yoshida (medical physicist) and Dachman (clinical radiologist) are in the extension of CAD to the detection of lung nodules in CT images of the thorax and the detection of polyps in CT images of the colon, respectively. The UCCRC has also fostered the collaborative efforts in genetic research and quantitative image analysis. For example, Dr. Giger has extended her work on the computerized analysis of mammograms to include texture analysis and is collaborating with Dr. Olopade, a medical oncologist, on correlating measures from such analysis with women at high risk for developing breast cancer. Initial results indicate that radiographic texture analysis can distinguish between women at low risk and those who are BRCA1 carriers. In addition, studies are now underway to use the radiographic markers in studying women on tamoxifen and those not on tamoxifen. Other examples of the collaborative research fostered by this program are those between Dr. Giger and Dr. Heimann, a radiation oncologist, on computer-extracted feature analysis for prognosis in breast cancer detected mammographically and between Drs. Armato and MacMahon in chest imaging and Drs. Vogelzang and Kinder in the mesothelioma clinic to define mesothelioma growth rates. Such collaborations are crucial in order for computerized analysis to be proven to be of clinical benefit, since development of successful image analysis methods depends greatly on knowledge of the physical image acquisition system (contributions from the medical physicists) as well as on knowledge of the characteristics of the normal anatomy and associated pathological states (contributions from the radiologists, oncologists, and cancer biologists).

In addition, advances in the development of new image acquisition methods have been fostered by interactions within the UCCRC. For example, Dr. Karzmar (physical chemist) and Dr. Bick (clinical radiologist) are investigating new magnetic resonance imaging sequences for magnetic resonance imaging spectroscopy for improved depiction of the presence and stage of disease. Dr. Halpern (medical physicist) and colleagues in radiation oncology are investigating in vivo EPR oxymetric imaging in order to better define selected aspects of tumor/tissue physiology and its response to toxins including radiation and chemotherapeutic agents.

The importance of the Advanced Imaging Program in the UCCRC is apparent in the strong commitment of the imaging scientists to innovative independent cancer research, and in their strong collaborative research with cancer biologists and clinicians. Together this type of research indicates a necessary and vital role for the Advanced Imaging Program to enable state-of-the-art cancer research. The Program serves as a mechanism for the transfer of imaging technology to all branches of cancer research within the UCCRC.
A. INVESTIGATION OF NEW METHODS FOR COMPUTERIZED IMAGE ANALYSIS

1. Computer-Aided Diagnosis in Breast Imaging

Drs. Nishikawa and Giger and mammographers in Radiology are working together in the development and testing of computerized methods for the detection and diagnosis of mammographic lesions. They have developed computer-ized techniques to assist radiologists detect and diagnose breast cancer on mammograms. The investigators have analyzed over 25,000 screening cases using their automated detection schemes for masses and clustered microcalcifications, and have performed follow-up analyses on the first 12,500 cases. Eighty-one women in their study cohort developed breast cancer. The investigators conclude that in a non-prevalence screening population, their computer-aided detection schemes are capable of detecting up to 50% (12/23) of screening-detected cancers a year or more before detected by the radiologist.

Mammographic mass lesion analyzed by the computer method, which yielded an estimated likelihood of malignancy of 97%. (Courtesy of Drs. Huo and Giger)

2. Computer-aided Diagnosis in Chest Radiography and CT

Although various investigators are now reporting methods for the computerized detection of pulmonary nodules in chest radiographs, many of the existing schemes suffer from a large number of false positives. Drs. Yoshida, MacMahon, and Doi developed a method for reduction of false positives based on radiologists' visual analysis strategy that uses normal anatomic structures as a guide for identifying abnormal structure.

3. Virtual Colonoscopy (Colonography) and Image Analysis

Drs. Dachman, Yoshida, and MacEneaney are developing a computer-aided diagnosis (CAD) scheme for the automated detection of polyps in virtual colonoscopy (CT colonography). This novel 3-dimensional CAD scheme first identifies the polyp candidates based on the volume curvatures calculated from the volume data acquired by a CT scan of the colon of a patient. Then, several geometric features are extracted from the candidates, and they are combined by an artificial neural network to detect polyps. Once completed, such a CAD scheme will potentially improve the early detection of colon cancers, advance the clinical practicality of CT-based colon cancer screening, and lead to reduced mortality due to colon cancer.

Computer detection of polyps on colonography (courtesy of Drs. Yoshida & Dachman)
4. Computer Classification of Focal Liver Disease on Ultrasound

Dr. Yoshida is investigating the potential of computer analysis in the classification of malignant and benign focal liver disease seen on ultrasound. The advantages of ultrasound in imaging focal liver lesions are well known; they include safety, relative accuracy, low cost, and availability. However, it is difficult to distinguish between benign and malignant lesions sonographically; additional, more expensive imaging (CT, MRI, and scintigraphy), or a biopsy (which has the risks of bleeding and infection) must often be used. In this study, a novel method of multi scale echo texture analysis was developed to distinguish benign (hemangioma) from malignant [hepatocellular carcinomas (HCCs) and metastases] focal liver lesions in B-mode ultrasound images.

B. Development of new methods of image reconstruction

Drs. Pan and C.T. Chen are involved in the development of advanced methods and techniques for quantitatively accurate reconstruction and processing of medical images in nuclear medicine imaging, conventional and helical CT, ultrasound diffraction tomography, and magnetic resonance imaging. Applications of these methods and techniques may improve physician’s ability to better detect tumors and other abnormalities, and to more accurately measure important physiologic parameters.

C. Investigation of new methods of image acquisition

1. Magnetic Resonance Imaging

Dr. Levin is investigating fast Gd-enhanced carotid magnetic resonance angiography (MRA). The long-term objective of this research is to improve the diagnosis of carotid atherosclerosis, which is the cause of most strokes. Levin’s group hopes to accomplish this by developing a method of contrast-enhanced carotid MR angiography (MRA) that is more sensitive, more specific, and more practical than currently available MRA techniques.

2. Magnetic Resonance Imaging Spectroscopy

Dr. Karczmar and colleagues are developing proton MR imaging methods, which are sensitive to changes in tumor oxygenation caused by radiosensitizing agents. The sensitivity of MR to changes in oxygenation in tumors derives primarily from the effects of paramagnetic deoxyhemoglobin on water proton MR signals. They have shown a direct correlation between changes in tumor oxygen tension (caused by radiosensitizing agents) and changes measured quantitatively by oxygen microelectrodes. MR measurements show that radiosensitizing agents do not uniformly increase tumor oxygenation. In fact, in some tumor regions, MR measurements suggest that oxygen levels decrease. This effect has important clinical implications because it predicts that radiosensitizers may result in decreased response to radiation in some tumor regions and these desensitized regions may repopulate tumors following treatment.

Conventional T2-wtd image and T1-wtd image with fat saturation

Images were synthesized by calculating the:

1) increases in spectral amplitude in each voxel,
2) decreases in spectral amplitude in each voxel,
3) maximum change in water spectrum, and
4) voxels with increases and decreases in water spectrum.

(Courtesy of Dr. Karczmar)
D. Identification of imaging methods for oncology and for the evaluation of new cancer drugs

Drs. Pelizzari and Grzeszczuk have developed a method for using visualization of anatomical structures as a segmentation aid. This method has been adapted to aid in localization of radioactive source positions for radiotherapy treatment planning. J.S. Lee, C. Pelizzari, and G.T.Y. Chen have used locally developed volume rendering software (“Rendo 2000”) to investigate the feasibility and utility of visualization of lymph nodes in planning radiotherapy of head and neck cancer patients. Methods for automating the adjustment of rendering parameters and improved data preprocessing tools are under development.

Rendered view (left) and range image (right) from prostate seed implant CT
(Courtesy of Dr. Pelizzari)

E. Investigation of methods for the evaluation of imaging systems

Drs. Jiang and Nishikawa are involved in the development of methods for the evaluation of new image analysis methods. Besides the use of ROC analysis and observer studies as a tool in assessing the potential of quantitative image analysis, fundamental research in the methods for analyzing observer data is being performed. In distinguishing between cancerous and benign lesions in mammography, the ability to obtain a 100% sensitivity level for the classification of cancerous lesions is of more importance than overall accuracy (including both malignant and benign classifications). Thus, the area under the ROC curve is not as useful as it is with detection tasks. Thus, a new index related to the area at the 95% true-positive level is being investigated as a means to evaluate both human observers and computer-vision methods. In addition, methods to assess the intra- and inter-observer variation in the diagnosis of cancer with and without the use of computer analysis output is being investigated.
TRANSLATIONAL ACCOMPLISHMENTS

Various translational accomplishments and opportunities exist within the Advanced Imaging Program. Drs. Giger, Nishikawa, and Jiang (medical physicists) are collaborating with Drs. Jokich and Bick (mammographers) in the clinical validation and translation of computer-aided diagnosis for the early detection of breast cancer. Similar collaborations between Drs. Armato, Giger, and Doi (medical physicists) and Dr. MacMahon (clinical chest radiologist), and between Drs. Yoshida (medical physicist) and Dachmann (clinical radiologist) are in the extension of CAD to the detection of lung nodules in CT images of the thorax and the detection of polyps in CT images of the colon, respectively. Drs. Armato and MacMahon are collaborating with the mesothelioma clinicians on computer assisted measurements of mesothelioma rind. Dr. Giger has extended her work on the computerized analysis of mammograms to include texture analysis and is collaborating with Dr. Olopade, a medical oncologist, on correlating measures from such analysis with women at high risk for developing breast cancer. Initial results indicate that radiographic texture analysis can distinguish women at low risk from those who are BRCA1 carriers. In addition, studies are now underway to use the radiographic markers in studying women on tamoxifen and not on tamoxifen. This component of mammographic image analysis is also ready for translation to the clinical environment and pilot funding from the UCCRC is helping to fund a research nurse coordinator in clinical mammography for such a study.

Various advances in the development of new image acquisition methods have been fostered by interactions within the UCCRC involving both basic scientists and clinicians. Such interactions expedite the translation to clinical medicine. For example, Dr. Karczmar (physical chemist) and Dr. Bick (clinical radiologist) are investigating new magnetic resonance imaging sequences for magnetic resonance imaging spectroscopy for improved depiction of the presence and stage of disease. Dr. Halpern (medical physicist) and colleagues in radiation oncology are investigating in vivo EPR oxymetric imaging in order to better define selected aspects of tumor/tissue physiology and its response toxins including radiation and chemotherapeutic agents.

PLANS FOR PROGRAM DEVELOPMENT

The Advanced Imaging Program will continue to expand its collaborative and funding efforts in order to maintain its state-of-the-art level in imaging research and technology. The translational research performed in moving CAD in breast imaging to the clinical arena will be further extended to include other aspects of breast imaging as well as imaging of the chest and colon. New image acquisition techniques such as those of magnetic resonance image spectroscopy will be studied for potential translation from animal studies to beneficial clinical procedures. Continued efforts are being put forth for the expansion of PET imaging for both basic and clinical research. Besides extending its research in the digital analysis and visualization of radiographic images, future collaborative research will include the analysis of biological images, such as in genetic research, to expedite research and reduce human error.

Drs. Armato and MacMahon from the Advanced Imaging Program and Dr. Vokes from the Clinical and Experimental Therapeutics Program are planning to extend the computerized detection of lung nodule on low-dose spiral CT to a lung cancer screening program.

In addition, investigators are planning on submitting an application in response to a planned NCI/NIH RFA for the formation of a Radiologic Response Assessment Core Facility as a supplement to the CCSG. The RFA will serve as a good opportunity for Drs. Nishikawa and Jiang of the Advanced Imaging Program to continue their research on observer performance studies, intra- and inter-observer variability, and system evaluation.
PROGRAM 6:

CLINICAL CANCER GENETICS AND PREVENTION PROGRAM
PROGRAM LEADER: OLUFUNMILAYO I. OLOPADE, MB, BS, FACP

22 MEMBERS

OVERVIEW AND SCIENTIFIC THRUST

The overall objectives of the Clinical Cancer Genetics and Prevention program are to integrate and focus the work of investigators with established research programs and to foster new collaborative efforts to characterize molecular pathways that are relevant in carcinogenesis and therefore amenable to chemoprevention approaches. It serves as a base for many research interactions focused on understanding the molecular pathogenesis of cancer with the ultimate goal of developing new and improved methods for risk assessment, early detection and prevention of the disease. The program also includes a core of investigators with expertise in human genetics and behavioral research.

RESEARCH HIGHLIGHTS

With the recruitment of Dr. Andrea King to the Cancer Center, we are developing a new area in behavioral research focused on Smoking Cessation and Addiction. With Pilot funding from the Cancer Center, Andrea King, Ph.D., Assistant Professor, Department of Psychiatry developed a Pilot project “Primary Prevention in Urban African-American Smokers”. The objectives of the pilot project were to: 1) follow-up on a cohort of underserved, urban African American smokers receiving comprehensive smoking cessation treatment; 2) develop and implement a smoking cessation intervention targeted at young adult smokers; 3) conduct program planning and initiate community-based smoking cessation treatment in a new cohort of underserved minority smokers in the south Chicago neighborhoods; 4) facilitate data collection in an ongoing trial examining the opioid antagonist naltrexone as a adjunct to smoking cessation treatment.

In a basic science project related to naltrexone, Dr. Yuan in the department of anesthesia is studying the effect of methylnaltrexone in reducing oral-cecal transit time in humans. Methylnaltrexone (MNTX) the first peripheral opioid antagonist currently under clinical investigation, does not cross the blood-brain barrier, thus offering a potential benefit in treating opioid-induced gastrointestinal side effects without interfering with pain control.

A number of studies were initiated this year by Dr. Matthews’ whose primary research interests are in cancer prevention and control, cancer survivorship, psychosocial adjustment to illness, and factors associated with mental and physical health outcomes among minority and other underserved populations.

Data collection for a study examining factors associated with information seeking and treatment decision among a sample of African Americans and Caucasians with a history of breast, prostate, and colorectal cancers is currently ongoing (NCI, RO1CA77525). Eligible participants within 24-months of diagnosis are identified and enrolled for the study through the Illinois State Cancer Registry.

The Relationship between Depression, Perceived Cancer Risk, and Cancer Worry among African American Breast Cancer Survivors. The purpose of this study was to examine the relationship between depression, perceived cancer risk, and cancer worry among African American breast cancer survivors presenting at a university medical center cancer risk clinic.

Dr. Olopade initiated collaborations with members of the School of Social Science Administration to develop a Center for the study of Health Disparities in Breast Cancer. In collaboration with Drs McClintock, Gelhert and Masi, they are examining psychosocial predisease pathways and breast cancer.
EARLY PHARMACOLOGY OF CHEMOPREVENTIVE AGENTS

Dr. Gustin was recruited in July of 2002 in order to expand our early pharmacology program to include focused efforts in chemopreventive agent development. Dr. Gustin joined us from the University of Illinois at Chicago where he was an integral part of their Phase I Chemoprevention Program. He was in charge of the design, implementation and coordination of NCI-supported Phase I studies of the antioxidant Lycopene in healthy as well as high-risk populations (prostate cancer). He continues to contribute to those studies as a clinical consultant and is currently preparing a manuscript that will summarize the results of a Phase Ia study of lycopene (food-based formulation).

Dr. Gustin’s major initial efforts after his arrival to the University of Chicago were directed towards creating a platform that would facilitate the conduct and implementation of state of the art early pharmacology studies of chemopreventive agents. The early pharmacology chemoprevention program is being built as an extension of our well established Experimental Therapeutics and Pharmacogenomics Program (Dr. Ratain). As such, most of the basic resources that support analytics (drug levels), pharmacokinetics, pharmacodynamics and clinical trial implementation and monitoring were already in place. His major initial concerns were then to maximize the ability of our institution to gain access to products under preclinical development (by the NCI and others), as well as to develop favorable links with other academic institutions with well-developed preclinical and clinical chemoprevention programs, in order to enhance scientific interactions.

In August of 2002, the University of Chicago joined efforts with a number of large academic institutions in New England (Dana Farber Cancer Institute, Dartmouth) and in the Midwest (University of Michigan) as well as outside of the United States (Leicester, England), to conform an International Consortium of academic centers that would provide a scientific and clinical platform for the design and implementation of Phase 1 and Phase 2 Clinical Trials of Cancer Chemopreventive Agents.

COLORECTAL CANCER PREVENTION

Dr. Bissonette is investigating the roles of bile acids in the promotion or inhibition of colon cancer. In the azoxymethane (AOM) model of experimental colon cancer, cholic acid potently enhances colon cancer, whereas ursodeoxycholic acid (UDCA) inhibits tumorigenesis. Similar actions are strongly suggested in humans, in whom high fat diets that are associated with increased cholic acid, enhance colon tumor risk.

Dr Chang is studying the mechanisms responsible for the intestinal epithelial cytoprotective properties of interleukin–11(IL-11) in models of intestinal injury and intestinal malignancies.

BREAST CANCER PREVENTION

Dr. Greene is studying the mechanism of action of female steroid hormones and nuclear receptors with the goal of developing and characterizing novel SERMs for HRT and breast cancer treatment and prevention. The overall goal of Dr Greene’s research is to determine the molecular mechanisms by which female steroid hormones regulate development, differentiation and/or cellular proliferation and survival in hormone responsive tissues and cancers.

Dr. Olopade’s laboratory has been studying cooperating oncogenes involved in BRCA1 tumor progression. They have examined whether amplification of HER-2/neu contributes to the aggressive biology of BRCA1-associated tumors.

Dr Grdina’s program remains focused on developing new effective strategies to prevent therapy induced secondary cancers in patients having a good prognosis and a relatively long life expectancy. Their research focus has expanded to include the investigation and development of novel approaches to the sensitization of tumors to radiation therapy and the prevention and treatment of metastatic disease.
PLANS FOR PROGRAM DEVELOPMENT

The Clinical Cancer Genetics and Prevention program is now a well-staffed fully integrated program with strengths in cancer genetics, risk assessment and screening, and translational studies in chemoprevention. A key area for future development is acquiring expertise in cancer genetic/molecular epidemiology. Of high priority, additional faculty with expertise in genetic and statistical epidemiology will be recruited to facilitate development of new methodologies for family studies, linkage and mapping studies and molecular epidemiological association studies. We will continue development of ongoing disease-specific research groups – breast/ovary, colon, prostate by recruiting more investigators with basic science expertise and create a new working group in health outcomes. A focus on cancer genetics will be maintained in all research areas, specifically incorporating the use of new technologies. In addition, we will deepen our commitments to reducing the disparities in cancer burden in minorities by expanding our research in Africans and African American populations.
FACILITIES OF THE PAST
BIOSTATISTICAL CORE FACILITY

Scientific Facility Director: Ronald Thisted, Ph.D.
Technical Facility Director: Theodore Karrison, Ph.D.

The Biostatistical Core Facility is a shared resource that provides collaborative support to University of Chicago Cancer Research Center (UCCRC) investigators in the design, conduct, and analysis of prospective clinical trials, population-based studies, observational studies, and basic science (laboratory and animal) research projects. The facility is directed by Dr. Ronald Thisted, Chair, Department of Health Studies. Dr. Theodore Karrison, Research Associate (Assoc. Prof.) in the Department of Health Studies, is the technical director. As stated in the original grant submission, the specific aims and objectives of this facility are to:

- collaborate in the development and execution of prospective, investigator-initiated phase I, phase II (and when needed phase III) and correlative/translational clinical protocols and provide statistical analyses of the data arising from those studies
- assist in the design and analysis of basic science and animal research experiments
- provide database development and management support to ensure the accuracy, timeliness, and quality of data submitted for analysis
- collaborate in the design and analysis of retrospective, investigator-initiated studies addressing clinical questions
- collaborate with investigators on the preparation of manuscripts for publication
- assist in new grant submissions
- participate in the teaching and training of investigators in fundamental statistical concepts, study design, clinical trials, and basic statistical methods, and
- perform statistical methodological research related to Cancer Center activities.

DIGITAL LIGHT MICROSCOPY

Scientific Director: Janis Burkhardt, Ph.D.
Technical Director: Shirley Bond

The Digital Light Microscopy (DLM) Facility continues to function as a user-based core providing state-of-the-art, or otherwise prohibitively expensive, microscopy imaging capabilities to all university investigators. The facility provides a valuable service to the university community by furnishing high quality instrumentation for microscopy and image analysis. In addition, maintaining the equipment in optimal condition requires skilled technical personnel, which individual laboratories typically cannot justify. Because imaging technology and computational capacity are evolving so rapidly, it is extremely difficult for individual researchers to maintain cutting-edge capabilities. By contrast, the facility can upgrade regularly and expand its capabilities depending on the direction of the investigators’ work. The facility also extends the research capacity for labs that have their own microscopes but have more users than it can accommodate. The capabilities provided by the facility are unique on the University of Chicago campus. Given the increasing reliance of many areas of cancer research on microscopy-based techniques, the facility is crucial to the scientific needs of UCCRC investigators.

Our continued aims are:

Provide well-maintained microscopes equipped for histology and DIC imaging, and digital-deconvolution and laser-scanning confocal imaging for fixed specimens as well as for living cells maintained under physiological conditions.

Provide computers and software for image analysis; including morphometry, 3D rendering, tracking of cell movements, and expert advice on all aspects of the user’s experiment from planning through publication.

Educate the university community in the use of current microscopy techniques and to complement services provided by other core facilities, including the UCCRC histochemistry and EM facilities.
DNA SEQUENCING CORE FACILITY

Scientific Director: Edwin Cook, Ph.D.
Technical Director: William J. Buikema, Ph.D.

Over the past year, there has been a change in leadership of the DNA facility. The previous Scientific Director, Dr. Haselkorn stepped down, the UCCRC facility was merged with the Psychiatry Department DNA Sequencing and Genotyping facility, and Dr. Edwin Cook assumed the role of Scientific Director. Dr. Buikema remains as Technical Director assuring continuity and excellence of service to cancer center members.

The DNA Sequencing Core Facility was established in the latter part of 1995 to serve a growing need in the University community for rapid and reliable DNA sequencing. The DNA Sequencing Core began as a shared facility with the Haselkorn laboratory, which was beginning to complete genomic sequence of Rhodobacter capsulatus. The first ABI 377 machine was obtained by Robert Haselkorn via a grant from the DOE in late 1995, while the second 377 was purchased by the Cancer Center a few months later and the loan paid off by the facility over the following five years. After the Rhodobacter project ended in 1999, the facility has primarily serviced the University community. A separate DNA Sequencing and Genotyping core facility was started in the Department of Psychiatry with an ABI 3700 and a LBL fluorescence polarization plate reader. With the support of the UCCRC and the Dean’s office, these two facilities merged in January 2002 and relocated to the Jules F. Knapp building basement (rooms R022 and R021).

The DNA Sequencing Core Facility provides primarily full-service DNA sequencing (i.e. reactions, cleanup and gel electrophoresis) of plasmid and PCR templates. Results (typically 600-800 bases) are provided online within one to two days of sample submission.

ELECTRON MICROSCOPY FACILITY

Scientific Director: Anthony P. Mahowald, Ph.D.
Technical Director: Edward K. Williamson, Ph.D.

The Electron Microscopy Core Facility (EM) continues to assist members of the UCCRC and other faculty and students at the University of Chicago to obtain ultrastructural information for approved research projects. The Core is organized to perform a variety of transmission and scanning electron microscopic procedures. The focus has been on immunolocalization using both cryo-ultramicrotomy and resin-based techniques. Modern equipment, including both transmission and scanning electron microscopes, is dedicated to Core utilization. Equipment for the use of the transmission electron microscope include two ultramicrotomes, including one that has a dedicated units for cryo-sections used in cryo-immunolabeling. We have full access to a Philips EM120 with cryostage for imaging macromolecules to obtain images suitable at 5-nm resolution. Instruments for the scanning electron microscope include, a recently purchased sputter coater (from cancer center funds), critical point dryer, and a digital scan generator, which allows digital, photographic, or both types of images to be collected and stored. The facility is equipped with a full darkroom, and several evaporators for general usage. We also have access to a Zeiss Photis scanner, which transfers images to a CD-ROM-writer for digital image archiving and morphometric analysis.
HUMAN IMMUNOLOGIC MONITORING FACILITY

Director: Thomas F. Gajewski, M.D., Ph.D.

Technical Director: Helena Harlin, Ph.D.

The purpose of the Human Immunologic Monitoring Facility is to perform such assays in the context of clinical trials in cancer patients. This service enables a range of clinical cancer researchers, who may not themselves have the expertise or laboratory commitment to carry out these assays, to measure immunologic endpoints in participating study subjects.

Current Assays and Procedures

- Antigen-specific T cell function by ELISpot
- Tetramer analysis
- PHA-stimulated T cell proliferation
- Serum analysis of cytokines by ELISA
- Flow cytometric analysis of hematopoietic and T cell subsets
- Induced intracellular cytokines by flow cytometry
- RNA preparation for quantitative RT-PCR and gene array screens
- Quantitative RT-PCR for immunologically-relevant genes
- Under development: Antibody-dependent cell-mediated cytotoxicity (ADCC), Immunohistochemical analysis of tumor biopsies (e.g. expression of HLA, TAP, tumor antigens, apoptotic cells)

IMMUNOLOGY APPLICATIONS CORE FACILITIES

Scientific Director: Anne Sperling, Ph.D.

Technical Director: Bart Eisfelder, Ph.D.

The Immunology Applications Core Facility (IACF) is comprised of the Flow Cytometry Facility, Immunohistochemistry Facility, and the Fitch Monoclonal Antibody Facility. The facilities, designed to meet the need for custom cytologic analysis, continue to respond to the demand for new and improved technology. The integrated facility has three goals: 1) provide cutting-edge technology and expertise; 2) pursue technology and application development; 3) education. The first goal is attained with state-of-the-art instrumentation and continuing education for the expert personnel in each area. Application development involves close relationships with Cancer Center researchers who are continually looking for new methods to address their scientific questions. The educational goals are satisfied by providing application workshops, training sessions, and one-on-one protocol development and consultation. The facility has an extensive reference library containing references pertinent to the technological focus of the facilities.

The facilities, utilized by Cancer Center Researchers in many areas of study, serve basic research in cellular structure/function, as well as translational research in clinical applications and molecular medicine. The Flow Cytometry Facility provides analytical detection and sorting of single-cell suspensions and subcellular components using multi-parameter fluorescence technology. The Immunohistochemistry Facility provides cellular detection within the context of the surrounding tissue. The Fitch Monoclonal Antibody Facility provides the antibodies necessary for the detection of cells and subcellular components.
LASER CAPTURE MICRODISSECTION (LCM) CORE FACILITY

Scientific Director: John Hart, M.D.

Technical Director: Maria Tretiakova, M.D., Ph.D.

The LCM Core Facility was established in January 2001 as a joint venture by the Department of Pathology and the UCCRC, with the full support of the Biological Sciences Division. The facility offers special expertise in the capture of targeted cell populations (from human and animal tissue sources) using the best available instruments and techniques. High quality preparations of DNA and/or RNA extracted from these selected cell populations are returned to the investigator for various downstream applications. The isolation and enrichment of a particular cell type is essential to the success of many newly developed molecular techniques, such as gene expression by cDNA and oligonucleotide microarrays.

The LCM Core facility provides the following services:

Sectioning of paraffin and frozen section tissue blocks:
The section of Surgical Pathology maintains a complete archive of paraffin blocks from all specimens received over the past 40 years on site within the department. This resource is managed by the HTRC Facility. Likewise, frozen section blocks of normal and tumor tissue are stored within the department and maintained by the HTRC facility. These paraffin embedded or frozen tissue specimens are sectioned utilizing protocols specifically tailored to the requirements of the LCM instrument.

Laser capture microdissection of targeted cells:
Laser capture microdissection is performed utilizing either the Arcturus PixCell II or Leica AS LMD instrument. The Arcturus instrument is equipped for detection of immunofluorescent labeled targets as necessary. Together these instruments are widely considered to represent the best available technologies for LCM. Immunohistologic and immunofluorescent labeling of tissue sections are offered as a service by the HTRC Facility.

Archiving of LCM images:
Digital images of all tissue sections before and after microdissection, and of the captured target tissue samples are maintained on site and are available to investigators on Zip disc, CD disc or via e-mail. These images provide documentation of correct target cell capture and represent a quality control measure. They are also useful to investigators in preparing manuscripts for publication.

Isolation of DNA and RNA:
DNA is isolated from the captured target samples utilizing the Invitrogen DNAeasy kit or the Arcturus/NIH protocol optimized for very small sample size. Likewise RNA extraction from microdissected samples is performed using either the MiniRNA or Nanoprep Kit (Stratagene), Picopure RNA isolation Kit (Arcturus) or the NIH protocol.

Quantification of DNA and RNA samples:
Performed upon request to confirm the presence of genomic material and provide quantification as a basis for the downstream analyses to be performed by investigators. Quantification is performed using the Spectrophotometer or DotMetric Assay (Geno Technology) for DNA or RNA. For quality assurance the Agilent microphoresis instrument is used (housed in Functional Genomics Core Facility).

Training of laboratory personnel in the use of the LCM instrument:
Investigators who wish to perform microdissection of tissue sections on their own will be trained in the proper tissue preparation for laser microdissection, operation and maintenance of the instruments, and the image archiving work station.
MAGNETIC RESONANCE IMAGING AND SPECTROSCOPY (MRIS) CORE FACILITY

SCIENTIFIC DIRECTOR: GREGORY KARCZMAR, PH.D.
TECHNICAL DIRECTOR: JONATHAN RIVERS, B.A.

The MRIS facility became an established Core in February of 2002 and provides MR imaging and spectroscopy support for Cancer Center Research. This includes studies of both animal models of cancer and patients. The MRIS Imaging facility contains a 4.7T magnet for imaging and model systems to investigate mechanisms of disease and aid in the design of methods that can later be implemented on clinical systems. In addition, the facility provides an important teaching resource, aiding graduate students, residents and postdoctoral fellows to develop a thorough understanding of all areas of biomedical research and provides a powerful new research tool for investigators throughout the University campus.

OLIGOPEPTIDE SYNTHESIS-SEQUENCE FACILITY

Scientific Director: Nancy B. Schwartz, Ph.D.
Technical Director: Giridher Reddy, Ph.D.

The objective of the Peptide Synthesis and Sequencing Facility is to provide primary structural data on various proteins and peptides under study by members of the Cancer Center, other University of Chicago faculty as well as outside investigators.

Services currently provided include amino acid analysis or composition of proteins, amino-terminal sequence analysis of proteins/peptides, the production of synthetic peptides, and mass spectrometry for structural elucidation. In addition, the facility provides individualized consultation to Cancer Center researchers to enable them to design, synthesize, sequence and analyze peptides, as well as workshops for interested staff and faculty.

Peptide Synthesis  The use of the peptide synthesizer enables investigators to obtain custom-made peptides in the shortest time at the lowest cost with maximum versatility and, most importantly, to benefit from on-site consultation on peptide design and pre- and post-purification strategies.

Protein Sequencing  Sequence information for particular proteins is necessary for preparing oligonucleotide probes for the purpose of cloning cDNA; in the study of posttranslational processing (including glycosylation, phosphorylation and proteolytic cleavage) of both native and recombinant proteins; and in many active site and chemical modification studies designed to define the structure-function properties of enzymes and other proteins.

Amino Acid Analysis  Amino acid analysis enables the determination of the amino acid composition and the quantification of the samples for both synthesized peptides as well as samples prior to sequencing.

Mass Spectrometry  Mass spectrometry is available for the identification of nucleotides, peptides, proteins and post-translational modifications. In addition, it can serve for monitoring the peptide synthesis chain assembly process for optimization and maximization in the production of high quality, high yield and high purity synthetic peptides and for monitoring protein-protein interactions.
PHARMACOLOGY CORE FACILITY

Scientific Director: M. Eileen Dolan, Ph.D.
Technical Director: Jacqueline Ramirez

The major objectives of the Pharmacology Core Facility are to evaluate pharmacokinetic, pharmacodynamic and pharmacogenetic parameters in conjunction with clinical trials. The Facility is comprised of an Analytical Core and a Biochemical Core. The Analytical Core is responsible for measuring drug concentrations in biological specimens and modeling the pharmacologic data generated. The Biochemical Core is responsible for evaluating biochemical measures of drug activity or drug resistance including assays of pharmacological targets, and isolation of lymphocytes, DNA, and RNA.

SCIENTIFIC VISUALIZATION AND IMAGE ANALYSIS CORE FACILITY

Scientific Director: Maryellen L. Giger, Ph.D.
Technical Director: Chun Wai Chan, M.S.

The core facility contains state-of-the-art equipment for scientific visualization and image analysis. The facility serves the biomedical cancer research community at The University of Chicago and includes systems for real-time 3-D graphics & rendering, parallel computing and virtual reality. Real-time, local visualization capabilities enhance the research of basic scientists at the molecular, cellular and anatomic levels. In addition, the presence of such a core facility (under direction of the Advanced Imaging Program of the University of Chicago Cancer Research Center) fosters interactions and collaborations, as well as reducing the redundancies, of many investigative teams. It is important to note that the rapid evolution of computer technology may be expected in the future to allow routine, inexpensive clinical application of the techniques that can be developed now only by use of the facility.

The policy of the Scientific Visualization and Image Analysis Facility is to allow researchers to have free access to high-performance computer and visualization capabilities. This facility provides service for both investigators interested in extracting information from images (image analysis) and investigators interested in visualizing data obtained either from images or other exploratory means (scientific visualization). The facility provides some direct archival capabilities, however, many investigators provide their own archival means (disks) on the system that are then maintained by the core facility. The facility aids the research efforts of investigators working with images at the gross anatomical and physiological level as well as images of data from histological, cellular, and molecular levels.

TRANSGENIC MOUSE/EMBRYONIC STEM CELL FACILITY

Scientific Director: Fredric Wondisford, MD
Technical Director: Linda Degenstein, B.A.

The Transgenic Mouse Facility has been in operation at The University of Chicago since 1990. In 1996 the facility added embryonic stem (ES) cell technology as a service. Until mid 2002 the facility was under the direction of Dr. Elaine Fuchs. Dr. Fred Wondisford has recently taken over as Scientific Director of the facility due to Dr. Fuchs’ departure from The University of Chicago. The facility provides university-wide service for the generation of transgenic and ES cell technology mice.

The Core Facility is located in the recently renovated Cummings Barrier Facility. The facility is self-contained and consists of 3 rooms for housing mouse colonies and experimental mouse populations, 2 procedure rooms in the facility where embryo injections and surgical implantation of embryos take place, and a cage washing/sterilizing room for the preparation of clean caging. An additional room will be opened in 2003 for special strains of mice to be used in the facility.
CLINICAL TRIAL PROTOCOL REVIEW AND MONITORING SYSTEM (PRMS)

Chairman: Daniel Haraf, M.D.
Vice Chairman: Walter M. Stadler, M.D.
Coordinator: Kelly McGinty

The primary activities of the Clinical Trial Review Committee (CTRC) have not changed significantly in the past year. All cancer related protocols initiated or conducted at the University of Chicago, including industry sponsored and investigator initiated studies are reviewed. Protocols that have already undergone peer review (e.g. CALGB, GOG, RTOG, NCI) are also reviewed by the CTRC. This policy ensures the CTRC is aware of all clinical trials for each disease site and to enable the CTRC to more effectively monitor prioritization. This policy also helps limit the number of conflicting protocols.

The CTRC has taken on one new responsibility. We now review amendments to existing protocols. The Chairman or Vice-Chairman of the CTRC reviews all amendments submitted through the data management office. The Chairman and Vice-Chairman have the option of bringing questionable amendments to the full committee if problems are identified.

In addition, based on the recently approved UCCRC institutional Data and Safety Monitoring Plan, at the time of protocol submission, for each protocol the CTRC will also:

A. Assess adequacy of data and safety monitoring plans (including audit procedures and frequency)

B. Determine level of study risk (criteria described in PDMO write-up) and recommend frequency with which study is to be audited. The list of protocols, level of risk and recommended auditing is sent to the QA Coordinator.

C. Verify that the protocol is assigned to a weekly safety monitoring conference.

D. Perform annual protocol renewals to ensure compliance with proposed DSM plans; reviews documentation that audits has been carried out as per CTRC recommendations.

The CTRC continues to meet every month to review protocols. A table reporting the number of protocols reviewed each month and the decision of the Committee is included for review. Stringent protocol review prior to CTRC submission helps to insure most protocols are approved or approved with revisions. All protocols undergo a biostatistical review and receive a review by Clinical Pharmacology prior to submission to the CTRC. These two areas were the most common reasons for requests for revision or protocol deferral. This preliminary review has reduced the number of deficiencies noted in the protocol at the time of the CTRC review.
CANCER CLINICAL TRIALS OFFICE (CCTO)

Scientific Facility Director: Marcy A. List, Ph.D.
Technical Facility Director: Rebecca Malloy R.N. B.S.N.

The Cancer Clinical Trials Office (CCTO) of the University of Chicago Cancer Research Center (UCCRC) is a shared resource that provides central management and oversight functions for coordinating, facilitating, and reporting on the cancer clinical trials of the University of Chicago. It interacts closely with the Biostatistical Core Facility (BCF) and the Protocol Review and Monitoring System (PRMS) to maintain high quality data, regulatory compliance, and centralized lists of active protocols with accrual status for use by UCCRC investigators.

The specific aims of the CCTO are:

- To facilitate and coordinate review and approval of protocols by both the UCCRC Clinical Trials Review Committee (CTRC) and the University of Chicago Institutional Review Board (IRB), and maintain records of correspondence with both committees.

- To monitor data quality and protocol compliance by periodic audits of all in-house protocols.

- To assure patient safety and regulatory compliance with Federal guidelines for investigational drug use and toxicity reporting through protocol audits and a centralized Adverse Event (AE) reporting system which confirms that all appropriate NCI and other agencies are notified of serious events.

- To facilitate Federal reporting requirements such as CDUS reports on phase II network trials and annual IND reports.

- To provide a centralized database of active studies and patients accrued to cancer clinical trials for use by investigators and the PRMS.

- To provide the centralized regulatory and data management coordination needed for the conduct of studies through a network of affiliated institutions.

- To provide training and education to new investigators, nurses, and data management personnel in the technical aspects of clinical research and good clinical practice.
CANCER CENTER MEMBERS
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<th>LAST NAME</th>
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<td>Herbert T.</td>
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Mitchell Posner, M.D.,
Professor, Department of Surgery, Section of General Surgery

Peggy Baker, LCSW,ACSW, Director, Cancer Program Development

Ramona Behrendt, LCSW,ACSW, Social Worker, Social Services Department

Eric Beyer, M.D., Professor, Department of Pediatrics, Section of Hematology-Oncology

Lorrie Elliott, M.D., Assistant Professor, Clinical Medicine, Primary Care

Daniel Haraf, M.D., Associate Professor, Department of Radiation & Cellular Oncology

Philip Hoffman, M.D., Professor, Department of Medicine, Section of Hematology/Oncology

Nora Jaskowiak, M.D., Assistant Professor, General Surgery, Department of Surgery

Rosalyn Johnson, RHIA, Director, Medical Records

Karen Kim, M.D., Associate Professor, Section of Gastroenterology

Michael Koetting, Vice-President, Planning

Thomas Krausz, M.D., F.A.C.Path., Professor & Director, Department of Pathology

Michele Kuhn, Director, Patient Safety

Beatrice Miller, RN, Oncology, Patient Services Sector

Rebecca Malloy, RN, Assistant Director for Clinical Operations, PDMO

Gita Rupani, M.D., Assistant Professor of Anesthesia and Critical Care

Jennifer Sepiol, MBA, RHIA, CTR, Manager, Cancer Registry

Deepti Singh, M.D., Instructor, Department of Medicine, Section of Hematology/Oncology

Mitchell Sokoloff, M.D., Assistant Professor, Urology

David H. Song, M.D., Assistant Professor, Section of Plastic & Reconstructive Surgery

Nicholas Vogelzang, M.D., Director, Cancer Research Center

S. Diane Yamada, M.D., Associate Professor, Department of Obstetrics & Gynecology
Our mission is to provide superior health care in a compassionate manner, ever mindful of each patient’s dignity and individuality. To accomplish our mission, we call upon the skills and expertise of all our medical professionals, who work together to advance biomedical innovation, serve the health needs of the community, and further the knowledge of medical students, physicians, and others dedicated to caring.

WORLD-CLASS TREATMENT AND CARE

Today with so many changes taking place in the health care industry, individuals are becoming increasingly aware that not all hospitals—and not all physicians—are alike. There are differences. You should have options. That’s why you should become acquainted with the University of Chicago Hospitals and Health System and its physicians. We have been at the forefront of medicine for decades—quietly delivering extraordinary care to patients who come from all parts of the world. We have also been selected by U.S. News and World Report as one of the best hospitals in the United States.

This is where many of the country’s latest medical discoveries are made. Here, for example, there is a team of over 500 working to find better treatments for cancer. This is where physicians helped discover the dangers of cholesterol. Here, surgeons performed the nation’s first liver transplant from a living donor.

You see, there is a difference.

A CONVENIENT NETWORK OF CARING

More than just a hospital, the University of Chicago Hospitals and Health System consists of:

- Bernard Mitchell Hospital, the primary adult patient care facility;
- University of Chicago Children’s Hospital, devoted to the medical needs of children;
- Chicago Lying-in Hospital, a maternity and women’s hospital;
- Duchossois Center for Advanced Medicine, a newly opened outpatient care facility;
- Louis A. Weiss Memorial Hospital, a 225-bed hospital on Chicago’s North Side;
- The University of Chicago Physicians Group, a network of more than 600 University of Chicago physicians;
- CareMed Chicago, a home health care organization;
- Chicago Partners, Inc., a management services organization;
- Midwest Surgery Center, a state-of-the-art surgical facility in Palos Heights, IL;
- Affiliated physicians offices located throughout the Chicago area.
A PROVIDER OF SUPERIOR CARE

Here, where world renowned specialists treat a vast range of rare and serious illnesses, you may establish an ongoing relationship with a personal physician—a fine and sensitive doctor who will get to know you and your family.

You see, even for routine medical needs, it makes sense to be cared for by a doctor of such high caliber—a doctor who can refer you to any one of over 400 U of C board-certified specialists should the need arise. And remember, the best time to choose a personal physician is now—before you need one. Call 1-888-UCH-0200 for assistance.

EFFICIENT EMERGENCY TREATMENT

All emergency rooms are not alike. Featuring completely separate facilities for adults and children, the University of Chicago Hospitals offer excellent emergency room care from a highly trained staff. In fact, the pediatric emergency room is one of only a few pediatric trauma centers in the Chicago area.

Both emergency rooms are located at 858 E. 58th Street, at Drexel. In Chicago, to call an ambulance, dial 911.

A SINGLE PHONE CALL AWAY

It’s really quite easy to find out more about any of the services of the University of Chicago Hospitals and Health System. Simply dial 1-888-UCH-0200 and speak directly with one of our helpful, experienced operators. They can quickly arrange to match you up with a personal physician or specialist, or they can provide you with more information on screenings, classes or programs. They will even answer—or find the answer to—any health related questions or concerns you may have.

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TODD ZIMMERMAN, M.D.
Assistant Professor, Department of Hematology/Oncology

Adult Blood and Marrow Program

The adult blood and marrow program at the University of Chicago has undergone significant new scientific direction, reflecting the evolving field of stem cell transplantation and new leadership, Koen van Besien, M.D. Dr. van Beisen’s arrival on May 1, 2001, along with the new director of the stem cell lab, Amittha Wickrema, M.D., promises to result in significant new changes for the stem cell transplant program. As before, the hematologic malignancies, including lymphoma, multiple myeloma, and leukemia, account for the majority of the transplants which are performed both here at the University of Chicago and nationwide. The most innovative and substantial changes in the stem cell transplantation have been in the emerging technology of non-myeloablative or mini-allogeneic stem cell transplants. With this approach, the recipient receives an immuno-ablative dose of chemo/radiotherapy, which allows for engraftment of the donor’s stem cells. Bone marrow chimerism is achieved over a period of several months. This technique holds the promise of allowing engraftment of stem cells and theoretically the development of a significant graft versus tumor effect. This approach is currently being tested in a wide array of hematologic malignancies and select solid tumors such as renal cell cancer and malignant melanoma. Further follow up will be required in order to fully understand the potential clinical benefits of this modality. In addition to this, University of Chicago has recently applied and been accepted as a participant in the national marrow donor program. This promises to increase the number of transplants done allowing broader indications with matched unrelated donors (MUD). Furthermore, interest in the role of mismatched related transplants has again resurfaced at the University of Chicago, as new methods of T-cell depletion are explored.

Collaborative efforts continue in the investigation of new supportive care measures for patients undergoing stem cell transplantation. Clinical trials with anti-infective agents and new anti-fungals are currently underway as well as new therapies for the control of steroid resistant graft versus host disease. These trials promise to improve the outcome of our own patients as well as those patients nationwide in future clinical trials.
PHILIP C. HOFFMAN, M.D.
Professor, Hematology/Oncology

The Section of Hematology Oncology

The Hematology/Oncology Section in the Department of Medicine continues to see increased numbers of inpatients and outpatients with a variety of malignancies and hematologic disorders. There are active clinical research programs in most areas and involving many treatment modalities. In the past two years, we have recruited several new faculty members with particular interest in lymphoma, leukemia and bone marrow transplantation, leading to renewed vigor and excitement in those areas of oncology. The leukemia group manages patients with acute and chronic leukemias, including the use of allogeneic (involving a donor) bone marrow transplantation. A program has also begun offering bone marrow transplantation from matched unrelated donors. For leukemia patients who do not have a matched relative for bone marrow donation, this approach offers the option of marrow donation from concerned citizens who are part of an international bone marrow registry. Correlative laboratory analyses of peripheral blood and bone marrow are an integral part of the clinical research activity of this group. There has also been recent interest in “mini-allogeneic” transplantation, in which the immunosuppressive regimen is less toxic, and where the goal of therapy is to create an immune reaction against the tumor by the transplanted stem cells. The leukemia and lymphoma clinical teams collaborate closely with section members who focus on the laboratory aspects of cytogenetics and molecular genetics.

In the area of solid tumor oncology, there are multiple active programs. The chest oncology program is studying a variety of combined-modality treatment programs for locoregionally advanced lung cancer, utilizing concomitant chemotherapy and radiotherapy. In addition, trials using chemotherapy drugs along with some of the “targeted therapies”, i.e., those drugs which specifically target tumor cell growth factors in non-small cell lung cancer are in progress. New drugs are frequently being tested in Phase II trials for patients with widespread disease, in hopes of finding improved therapies. There are also protocols in place for the treatment of advanced esophageal cancer. This year, we have recruited two new faculty members to the chest oncology group with major laboratory interests in correlative science in lung cancer.

The head and neck oncology group is evaluating a number of concomitant chemotherapy-radiotherapy protocols in patients with advanced disease. Many patients can now be offered “organ-sparing” therapy, thus avoiding the sometimes disfiguring and voice-sacrificing surgery that such patients traditionally have undergone. Small targeted molecules are also being used as part of therapy protocols for these patients, as well.

The genitourinary oncology group is evaluating a large number of treatment protocols for patients with prostate cancer, with particular interest in developing new strategies for patients with advanced, hormone-resistant disease. In addition, they have been conducting multiple trials using newer biologic response modifiers (e.g., interleukins and interferons) and new chemotherapy drugs in patients with advanced kidney cancer. The gastrointestinal oncology group has been quite active in developing treatment protocols, generally testing new drugs, for patients with advanced colorectal, pancreatic, liver and bile duct cancers. Recent data supporting the use of angiogenesis-inhibiting drugs, e.g., bevacizumab, are being applied in this group of patients.

The breast cancer treatment group is assessing an aggressive trial of combined chemotherapy and radiotherapy in patients with locally-advanced breast cancer who are not suitable candidates for surgery. In addition, they are conducting trials of new drugs in both early and advanced disease, including trastuzumab (Herceptin), the first monoclonal antibody developed to treat selected patients with breast cancer. In the management of advanced melanoma, the first tumor vaccine developed at the University of Chicago is now undergoing clinical testing.

New drug development is a major priority of the Section of Hematology/Oncology. There is a very active Phase I drug development program, which has a contract with the National Cancer Institute to test new anticancer drugs. Phase I trials evaluate new drugs, or older drugs combined in a novel way with modulating agents, to determine the appropriate doses for subsequent testing in Phase II trials. At any given time, 10-15 trials of Phase I agents are underway. Though such trials do not yet have a track record in cancer treatment, they offer hope to patients whose cancers have failed to benefit from standard therapies, or for which there is no standard therapy. In the past few years, the Section has also had a large Phase II contract, to test new drugs at established doses in specific groups of cancer patients to assess their efficacy in cancer treatment. At any given time, 3-5 Phase II trials are underway. We have also recently recruited a new faculty member whose interest is in clinical trials of chemoprevention.
The Department of Surgery

The Department of Surgery and the section of General Surgery embrace three specific goals as their mission; (1) excellence in patient care, (2) creation of new knowledge through basic science and clinical research and (3) education. This mission is the foundation upon which the cancer program in the Department of Surgery continues to build and grow. There has been a long-standing commitment and tradition of excellence within Surgical Oncology and the past year has been marked by an extraordinary initiative in programmatic development and growth. A critical mass of individuals dedicated to patient care and research and education in Surgical Oncology are now in place.

Multidisciplinary clinics and conferences are the cornerstone of a departmental commitment to comprehensive treatment of cancer patients. These combined initiatives are already in existence for head and neck oncology, thoracic oncology, gastrointestinal oncology, breast oncology and bone and soft tissue sarcoma and melanoma. The department’s commitment to comprehensive, state-of-the-art care for cancer patients is reflected in the establishment of a center of excellence in minimally invasive surgery. Technologies and communication advances have now led to the use of less invasive and more “patient friendly” surgical procedures for the diagnosis, staging, treatment, and palliation of patients with a variety of solid tumors. Minimally invasive procedures for resection of cancers of the lung, esophagus, liver, colon, rectum, prostate and kidney, have been developed, refined and are currently being performed at the University of Chicago Hospitals. New faculty recruitments have further augmented the application of minimally invasive surgical approaches, as will the introduction of robotic technology in the management of a variety of cancers.

The educational component of the cancer program in the department of surgery is punctuated by three didactic conferences: (1) Surgical Oncology Case Conference that reviews on a weekly basis all cancer cases performed within the section of general surgery as well as a discussion of interesting and illustrative cases to provide an educational foundation in oncology for students, residents and fellows, (2) Surgical Oncology Journal Club in which controversial selected topics in surgical oncology are debated monthly by fellows and residents with an expert attending physician serving as a moderator for the subsequent discussion and (3) a Surgical Oncology Core Lecture Series which meets twice a month to cover the entire gamut of issues related to oncology.

These three conferences serve as the fulcrum of the core curriculum for our surgical oncology fellowship program. We are one of only thirteen programs approved by the Society of Surgical Oncology and recently received full five-year approval. The fellowship again underscores our commitment to excellence in patient care, education and research and serves as the training ground for leaders in academic surgical oncology in the future.

Above are highlighted only some of the events and issues that have occurred during the past year within the Department of Surgery. The upcoming year will evolve along the same direction that has made the Department of Surgery one of the recognized leaders in oncology in the nation.
The Department of Radiation Therapy

The Department of Radiation and Cellular Oncology continues to provide patients with excellent care. We are also trying to expand medical knowledge through basic science and clinical research. The field of radiation oncology is technically demanding and the technology available for patient treatment has shown rapid growth. These advances in technology have helped to expand the use of radiation treatment to an integral part of the cancer therapy armamentarium. Radiation therapy has evolved from the days of low energy radioactive sources through orthovoltage to the current treatment with high-energy linear accelerators. This has enabled the more effective treatment of deep-seated tumors. Prior to the days of linear accelerators skin toxicity limited the amount of radiation that could safely be given. Skin toxicity is seldom a problem with current treatment machines due to the physical characteristics of the radiation they produce. This allows the delivery of higher more effective doses to cancer bearing tissues.

The recent ability to use CT data for radiation treatment planning allows the radiation oncologist to more precisely define the cancerous area and delineate areas at risk for microscopic sub-clinical extension of tumor. The University of Chicago Department of Radiation and Cellular Oncology purchased a CT simulator for the Center for Advanced Medicine in 1997 to provide patients with the benefits of advanced treatment planning. Since CT based treatment planning has been shown to be superior to conventional treatment planning, we installed a second CT simulator and retired our conventional planning machine.

The use of CT based treatment planning has enabled the development of 3D conformal radiation therapy. This advance lets the treating physician shape the radiation more precisely to the shape of disease containing tissue. In addition, 3D planning systems permit a more uniform dose to be delivered. This reduces the chances of under dosing disease and enhances the likelihood of cancer control.

The latest technological advance has been the introduction of Intensity Modulated Radiation Therapy (IMRT). This advance was made possible by the latest generation of linear accelerators that have multi-leaf collimators that automate blocking in conjunction with the latest treatment planning software. This latest advance in technology enables the radiation oncologist to shape the high dose (damage causing) area of radiation to a degree that was not thought to be possible only a few years ago. In addition, the radiation oncologist can limit the amount of radiation passing through critical normal tissue. These enhancements in targeting cancer while limiting doses to normal structures should translate into better disease control and fewer long-term complications. The University of Chicago Department of Radiation and Cellular Oncology was the first center in Chicago to fully implement this treatment option and provide IMRT to its patients.

The list of disease sites treated with IMRT at the University of Chicago continues to grow. IMRT is the standard treatment offered to patients with prostate, anal, cervical, uterine, and pancreatic cancer. Dr. Mundt has been able to show the doses of radiation to normal small bowel and bone marrow can be significantly decreased with the use of IMRT in cervical and uterine cancer resulting in fewer toxicities.

Head and neck cancer is another area where IMRT has become the standard treatment technique. Here there are multiple critical structures involved in speech and swallowing packed into a confined space. This makes head and neck cancer an ideal site for IMRT treatment. The goal of treatment is to maintain the excellent control rates we have seen while reducing the long-term toxicity by precision radiation therapy.

The Radiation Oncology Department has remained active in multiple areas of clinical investigation. Members of our department participate in all the Tumor Conferences conducted at the University of Chicago. We are members of CALGB, GOG and RTOG. There are many active clinical trials that have been designed with the joint collaboration of medical oncology and radiation oncology.

Our latest initiative will explore integration of biologically active agents with radiation therapy. Protocols using tumor necrosis factor (TNF) with radiation have been activated for the treatment of pancreatic and esophageal cancer. Additional studies with TNF are being activated for patients with head and neck cancer.
LORRIE ELLIOTT, M.D.
Assistant Professor of Medicine, Section on General Internal Medicine

The University of Chicago Primary Care Group

The Primary Care Group consists of 37 faculty members who provide comprehensive general medical care for adults. Our role in cancer care runs the gamut from prevention and risk assessment to evaluating symptoms, diagnosing cancer, referral to appropriate specialists, coordination of care, medical care during cancer therapy, psychological support, and, when needed, addressing end-of-life issues.

One of our routine but most important roles is helping people prevent cancer. Simple advice on always wearing sunscreen may cut dramatically the number of skin cancers. A healthy, high-fiber, low-fat diet and regular exercise may play a role in preventing colon and breast cancers. Using condoms may prevent the transmission of human papillomavirus, which causes many cases of cervical cancer. Assisting people in quitting smoking using individual or group counseling and medications is paramount in preventing lung cancer. We also screen our patients for cancers that can be cured when caught early enough. Yearly mammograms and breast exams, PSA testing and digital rectal exams for prostate cancer, fecal occult blood cards and flexible sigmoidoscopy, skin exams for skin cancer, and yearly Pap smears and pelvic exams for cervical, uterine, and ovarian cancer are commonly performed screening exams. With the explosion in biomedical research in recent years we have an enormous amount of new information to give to our patients regarding cancer prevention, screening, and treatment. With the widespread use of the Internet, there has also been an increase in the amount of erroneous information available for patients. It is our job as internists to critically evaluate new data and distill that into useful and accurate information for our patients.

We are also active in cancer risk assessment. Again, understanding the scientific literature enables us to give a worried patient an accurate assessment of their true risk of cancer. With the identification of risk factors, we are able to help patients modify some risk factors and thereby cut their risk of cancer. We work closely with the Cancer Risk Clinic to identify and refer patients whose family histories may put them at an increased risk of cancer; the Cancer Risk Clinic then does in-depth genetic counseling and, when warranted, genetic testing.

As general internists, we are usually the first to evaluate a patient’s symptoms and perform the testing that leads to a diagnosis of cancer. This is a difficult and emotional time for patients and their families, and they rely on us for information about treatments and prognosis, psychological support, and trust us to refer them to the appropriate specialists. Our long-term relationships with our patients are particularly valuable at this time. During cancer treatment we continue to provide general medical care, coordinate referrals and therapy, and provide a source of support for our patients.

Many of our patients are cancer survivors, and it is a joy to see them embrace their cancer-free lives. Unfortunately, not all cancers can be cured. Again, our long-term relationships with our patients help make difficult discussions about advance directives more comfortable, and we become their partners in managing their end-of-life care. Together with the dedicated and caring hospice workers we provide symptom management, pain control, and emotional support.
Department of Obstetrics and Gynecology

The Department of Obstetrics and Gynecology (OB/GYN) consists of physicians who are general obstetrician gynecologists and those who specialize in the areas of maternal fetal medicine, reproductive endocrinology, urogynecology and gynecologic oncology. An OB/GYN is considered a primary care physician and, as such, may be the only physician that a patient sees for her routine medical care. The OB/GYN plays an important role in the prevention, diagnosis and, occasionally, the initial management of both gynecologic and non-gynecologic malignancies. During a medical visit, the OB/GYN will assess a patient's risk factors for the development of cancer, perform a physical examination, and order tests that screen for malignancies. A detailed family history may reveal that multiple members of a patient's family have breast and/or ovarian cancer, placing a patient at risk for the development of a hereditary breast and/or ovarian cancer syndrome. In this instance, the OB/GYN may play a significant role in the prevention of disease by recommending that a patient see a genetic counselor or be referred to the Cancer Risk Genetics Clinic to decide whether genetic testing for BRCA1 or BRCA2 mutations may be of value. If the patient is then deemed to be at significant risk for the development of ovarian cancer, the OB/GYN may recommend that a patient undergo a prophylactic salpingo-oophorectomy (removal of the tubes and ovaries) when child-bearing is complete to prevent the onset of ovarian cancer. This treatment is highly effective in preventing over 95% of cancers from developing.

The OB/GYN will also perform a detailed annual physical examination to include a breast exam, pelvic exam (which should include a rectovaginal examination), a Pap smear to detect cervical dysplasia (a potential precursor to cervical cancer), and, if appropriate, a test for occult blood in the stool, which may be a sign of colorectal cancer. Careful examination of the cervix may reveal a firm, nodular area characteristic of a cervical cancer. A rectovaginal examination is extremely important as it can detect endocervical cancers that are not visible to the naked eye because they have developed higher in the cervical canal. A rectovaginal exam can also detect pelvic masses, which may herald the presence of ovarian pathology, or uterine enlargement, which may be an indication of uterine pathology. Fecal occult blood tests are also performed in women over the age of 50 to screen for adenomatous polyps and colorectal cancer. For women over the age of 40, the OB/GYN follows the screening recommendations as put forth by the American Cancer Society and will order annual screening mammograms. For women over age 50, a flexible sigmoidoscopy, colonoscopy or barium enema will also be ordered to screen for polyps and colorectal cancer.

A frequent presenting complaint to the OB/GYN is abnormal or irregular vaginal bleeding. This may take the form of regular, but heavy menses, irregular menses, bleeding after intercourse or frank postmenopausal bleeding. The OB/GYN takes into consideration the patient's history and presenting complaints to assess whether this abnormal bleeding may be a sign of cervical or uterine cancer. Symptoms of ovarian cancer can be particularly difficult for the physician to attribute to a particular disease process as they include nonspecific complaints such as bloating, constipation, and/or abdominal pain. Once the OB/GYN performs the diagnostic work-up and determines that a gynecologic malignancy is present, s/he will typically refer the patient to a gynecologic oncologist who has subspecialty training in the treatment of gynecologic malignancies. The gynecologic oncologist can then perform any necessary surgery, administer chemotherapy and, in conjunction with a radiation oncologist, play an active role in deciding on radiotherapy treatment regimen. The gynecologic oncologists at the University of Chicago are members of the Gynecologic Oncology Group, a National Cancer Institute funded cooperative clinical trials group and, as such, encourage patients to participate in the nearly 20 clinical trials that are available for cervical, endometrial, ovarian, and vulvar cancers.

The OB/GYN and gynecologic oncologist work together to help prevent, diagnose and treat patients with gynecologic malignancies in an efficient manner to help produce an optimal outcome for the patient. This is carried out in a multidisciplinary manner utilizing the expertise of our radiation oncology and medical oncology colleagues. The importance of other professionals such as our chemotherapy nurses and social workers cannot be overemphasized as they frequently make significant contributions to the comprehensive care of our patients.
Approximately 12,400 children and adolescents under the age of 20 are diagnosed with cancer each year in the United States. Approximately 2,300 U.S. children and adolescents die of cancer each year, making cancer the leading cause of disease-related mortality for children aged 1 to 19. Major categories of childhood cancer include Leukemia, Lymphoma, Brain tumors, Neuroblastoma (Cancer of Sympathetic Nervous System), Retinoblastoma, Wilm’s tumor (Kidney), Hepatoblastoma (Liver), Bone cancers, Soft Tissue, Germ Cell, and Carcinomas.

The incidence of childhood cancer has increased slightly over the last 30 years. Approximately 150 children out of every million children younger than 20 years of age are diagnosed with cancer annually. On the other hand, the survival rate for children with cancer has improved substantially, particularly over the last 30 years. In 1975, approximately 50 percent of children with cancer survived 10 years from diagnosis. Recent data show that almost 70 percent of children with cancer now survive 10 years from diagnosis.
PEDIATRIC CANCER AT THE UNIVERSITY OF CHICAGO
– AN OVERVIEW

CLINICAL CARE

The Pediatric Hematology/Oncology program is a leader in Chicago, offering both conventional and investigational forms of therapy. The program is uniquely patient- and family-centered, with patients benefiting from a multidisciplinary approach to the care of cancer patients and their families.

The program is focused on providing the best possible care for our patients with the fewest hospitalizations. Whenever possible, children receive treatments on an outpatient basis in a brand new clinic and transfusion suite in the remarkable Center for Advanced Medicine.

When it is necessary for patients to be hospitalized, children and adolescents receive care in a dedicated hematology/oncology and bone marrow transplant unit.

From diagnosis through follow-up care, each patient is followed by a faculty physician from the University of Chicago, a dedicated, masters prepared Clinical Nurse Specialist, a pediatric oncology social worker, and a team of child-life specialists.

The Child Life and Family Education program provides emotional support and education for children and their families at the bedside, in the clinic and in a well-equipped and staffed playroom. Family support, as well as food and lodging, is also available at a nearby Ronald McDonald House.

The program has specific clinical and research programs in childhood cancer including leukemia, Hodgkin’s and non-Hodgkin’s lymphoma, brain tumors, soft tissue and bone sarcoma. State of the art diagnosis and treatment is provided for all blood diseases including aplastic anemia, sickle cell anemia, white blood cell defects, thrombocytopenia, and bleeding disorders.

The bone marrow transplantation program, with cord blood, allogeneic and autologous transplants, is a major regional center in the U.S. This program treats children with hematologic disorders such as aplastic anemia and hemoglobinopathies; oncologic disorders including leukemia and solid tumors; and genetic disorders including immunodeficiency syndromes, osteopetrosis and metabolic storage disorders. The program utilizes peripheral blood, placental blood and bone marrow as sources of stem cells for transplant.

The program is a full member of the Children’s Oncology Group, and participates in national and international research programs and clinical trials. The program is a site for the National Cooperative Sickle Cell Study and for the Illinois State Screening Program for Hemoglobinopathies.
RESEARCH

Clinical

The section of Pediatric Hematology/Oncology has an active and productive clinical research program. As full members of the Children’s Cancer Group, the section has 160 patients enrolled on 84 protocols. In 2000, the section enrolled 14 patients on such studies. Dr. James Nachman and Dr. Charles Rubin are among the leaders for a number of Children’s Oncology Group (COG) studies, including those for Hodgkin’s disease and acute lymphoblastic leukemia. Dr. Nachman has also chaired a limited institution pilot trial for osteogenic sarcoma.

Basic Science

The section of Pediatric Hematology/Oncology has an internationally recognized, federally funded basic science research program directed by Dr. Beyer. The focus of the research program is to investigate the process of intercellular communication, specifically, an understanding of the structure and function of gap junction proteins.

Understanding how cells communicate with one another may lead to better understanding of how to control the growth of cancerous cells.
The diagnosis, treatment and follow-up of patients with neoplastic disorders requires a dedicated and multidisciplinary team of health care professionals. At the heart of that team are the Clinical and Anatomic Pathology Laboratories, where the tests that are essential for the accurate diagnosis and optimal treatment of the patient are performed. At the University of Chicago, each clinical section of the Department of Pathology provides unparalleled diagnostic services to the patient with cancer and to the physicians who care for them.

Usually, the initial diagnosis of cancer is made on a tissue specimen or biopsy that is reviewed by the pathology staff of the Sections of Surgical Pathology or Cytopathology. In the case of lymphoma or leukemia, the diagnostic services are provided by the Hematopathology Section and the Clinical Hematology Laboratory. All of these areas provide a full range of consultative services and highly specialized studies, including expert morphologic analysis, flow cytometry, immunohistochemistry, and in situ hybridization studies in order to arrive at the correct diagnosis.

Each of the full-time surgical pathology faculty has one or more areas of special interest and expertise and serves as the pathologist of record for one or more of the institutional multidisciplinary cancer groups, which include chest, gynecologic, gastrointestinal, bone and soft tissue, head and neck and breast oncology groups. Surgical pathology faculty attending one or more of the specialty multidisciplinary cancer groups will, in turn, update their colleagues and outline for the residents necessary information for surgical pathology reporting that will impact on newer sub-classifications for staging and therapy decision making. Surgical pathology faculty interacts through multidisciplinary tumor groups as collaborators in ongoing clinical research studies, including treatment outcomes.

The surgical pathology faculty is responsible for examining all tumor resections to assist in providing fresh neoplastic and normal tissue samples being studied in a variety of institutional as well as national cooperative protocols. Additionally, the surgical pathology faculty facilitates all tissue acquisitions into the institutional frozen tumor bank.

Among the most recent advances in care are the recognition that a number of tumors are associated with specific genetic abnormalities that can be detected with appropriate probes. The Molecular Diagnostic Laboratory provides molecular assays for many of these genetic changes and also uses state-of-the-art molecular procedures to monitor for residual disease following cytotoxic therapy.

In addition, the laboratories provide many of the tools that are necessary in staging the spread of the cancer, in predicting prognosis and in monitoring the response to treatment. The initial evaluation and monitoring of abnormal bleeding and clotting disorders that are often associated with cancer therapy is done by the Coagulation Laboratory. The Clinical Hematology Laboratory monitors the changes in the hematologic values that often determine how much therapy a patient can tolerate. Routine chemical studies and immunochemical analyses of a variety of serum tumor markers performed by the Clinical Chemistry Laboratory permit physicians to monitor disease progression and therapeutic response to different treatment protocols. And the detection of a spectrum of microbes (especially bacteria, fungi and viruses) that are common but debilitating in immuno compromised patients is performed by the Clinical Microbiology Laboratory. Furthermore, the recognition that a bacterium, *Helicobacter pylori*, is strongly associated with the pathogenesis of some lymphomas, underscores the potential role of the microbiology laboratory as knowledge of tumorigenesis accumulates. Lastly, the Blood Bank not only provides blood product support for patients receiving chemotherapy but is also crucial to the bone marrow transplantation for pediatric patients.

In all of these laboratory areas, the faculty is conducting basic and applied research that will lead to better understanding of malignant processes or improved methods for cancer detection. The participation of the Pathology Laboratories and faculty in a multidisciplinary approach helps the University of Chicago provide the efficient, effective and up-to-date treatment for cancer patients.
The Oncology Care Center

The Oncology Care Center comprises three adult hematology/oncology units in the Bernard Mitchell Hospital. Nurses care for patients who have a variety of malignant diseases. Most patients who are admitted to these units are receiving treatment for their malignancy, and are usually participating in clinical trials. The treatments include chemotherapy, radiation therapy, and biologic therapy. There are some specific patient populations who are admitted to designated units. For example, patients with leukemia or patients who are undergoing bone marrow transplantation are cared for on 6NW. Patients with solid tumors who receive chemotherapy are admitted to 6NE. Patients with head and neck cancers who receive concomitant chemotherapy and radiation therapy are admitted to 6SW. Patients may also be admitted for supportive care such as pain management.

The staff work as a team to provide care that the patient and family require. The Case Manager coordinates the care of the patient with the physicians, nurses, and other members of the multidisciplinary team. Multiple disciplines are utilized extensively in management and support of oncology patients. These include dieticians, social workers, pharmacists, physical therapists, occupational therapists, chaplains, and other consultative services.

To meet the challenge of caring for acutely ill oncology patients, nurses attend educational presentations to become more knowledgeable about new treatments and symptom management. Staff nurses are encouraged to become Oncology Certified Nurses (OCN) by successfully passing the Oncology national certification examination. The Clinical Nurse Specialist coordinates and teaches the Hematology/Oncology Bridging and Chemotherapy Provider Courses that are provided to all Oncology nurses. The Clinical Oncology Pharmacist is also a resource for the nurses and physicians.
The scope and complexity of services provided in the outpatient oncology care setting at the University of Chicago Hospitals have increased steadily. In the last year, research nurses, nurse associates, clinical nurses and specially trained infusion therapy/apheresis nurses have assisted with the implementation of approximately 400 protocols along with numerous off-protocol treatments. Since most of the protocols support patients for the outpatient cancer nurse.

The Research Section of Hematology/Oncology has experienced numerous additions to the nursing team due to the increased volume of patients being seen, along with new protocols and studies. There are twenty-six research nurses and twenty-five data managers to support the research endeavors. With their help, patients are guided through the outpatient multidisciplinary treatment environment, decreasing the need for inpatient admission for chemotherapy treatments. Under the direction of Denise Friesema, R.N, the research nursing staff is responsible for the coordination of all aspects of patient care while on a clinical trial. Each research nurse is disease-specific focusing their oncology nursing specialty in one area of cancer. The research nurse is active in the outpatient clinic following patients on treatment along with providing educational information about the cancer and cancer therapies. The nurses are involved in many aspects of clinical research including Phase I, Phase II, CALGB intergroup and pharmaceutical studies.

Outpatients are provided treatments and care in the Infusion Unit by specially trained, chemotherapy infusion nurses. The Unit is a comfortable, bright, open, environment that can accommodate thirty patients and their family members at a time. During the last fiscal year, approximately 22,000 patients came to the Infusion Therapy/Apheresis Units for care. Fourteen chemotherapy-certified nurses along with clinical nurses and assistants staff these areas of care. The nurses’ broad-based oncology knowledge provides patients and their families with ongoing education about the drugs they are receiving, along with the prevention and/or management of possible side effects. Patient’s concerns and questions are addressed during each encounter while assessing symptoms or problems they may have experienced since their last treatment. Patient education remains a primary focus for ambulatory oncology nurses. Teaching and providing the patient with information helps to lessen the anxieties associated with cancer and its treatment. The outpatient infusion therapy nurse recognizes the complexity of each patient’s care and plans appropriate interventions involving the physicians, research nurses and the multidisciplinary cancer care team.

For the treatment of melanoma, the current seven protocols open are outpatient based. These treatments, in additional to the off-protocol treatments, are administered in the Infusion Therapy Unit.

Outpatient peripheral blood stem cell collection, for transplant patients, is performed in the Apheresis area of the Infusion Therapy Unit. This unit is staffed with specially trained technologies and the chemotherapy nurses from the Infusion Therapy Unit. This provides a recognizable consistency of care for the transplant patient since most of them have received previous treatments and care from the same nurses.

As outpatient care for the treatment of cancer continues to grow, the goals of ambulatory oncology nurses continue to focus on interventions that will benefit the patient, enhance the quality and outcomes of care and be cost effective. The Outpatient Cancer Nursing Program at the University of Chicago Hospitals is dedicated to the continual development and safe delivery of outpatient cancer care.
EMMANUEL SEMMES, BS PHARM., RPH
Investigational Drug Pharmacist

MARK MILLER, CPT
Investigational Drug Lead Pharmacy Technician

Co-author:

JEANNELL MANSUR, PHARM.D., FASHP

The Pharmacy Department

The Department of Pharmaceutical Services supports the cancer patient and the oncology program through the provision of myriad inpatient and outpatient services. The complexity of the cancer patient’s drug therapy regimen requires a special expertise on the part of those professionals who provide this service. The pharmacist involved in the preparation of chemotherapy or a prescription for a pain medication must understand and review the appropriateness of the drug preparation in relation to the patient’s needs. The Department provides pharmaceutical care to the cancer patient as an inpatient through its inpatient chemotherapy satellite pharmacy, to the outpatient cancer patient who requires more complex infusions through its Outpatient Chemotherapy Infusion Center Pharmacy, and to the cancer outpatient who requires the filling of prescriptions for continued use through its outpatient retail pharmacy. The retail pharmacy, located at the Center for Advanced Medicine, is open Monday through Friday from 9 a.m. to 5:30 p.m. and on Saturdays from 9 a.m. to 1 p.m.

The Outpatient Chemotherapy Infusion Center Pharmacy is located in the Center for Advanced Medicine and is open Monday through Friday from 7 a.m. to 6 p.m. During these hours the pharmacy is staffed by certified pharmacy technicians and registered pharmacists trained in the proper handling and preparation of chemotherapy drugs. The pharmacists also review chemotherapy orders based, in part, on guidelines developed by the Chemotherapy Task Force.

The Inpatient Chemotherapy Satellite Pharmacy is the focal point for the processing and preparation of all anticancer drug therapy originating in the hospital. This unique pharmacy satellite was created in response to the increasing complexity of chemotherapy drug regimens and pharmacy’s changing role and involvement in the care of the cancer patient. It provides a separate area for the oncology specialist and clinical pharmacist to review and process chemotherapy drug orders prior to preparation.

The clinical trials process is one of the driving forces leading to the development of new drugs. At the University of Chicago Hospitals, there is ongoing research involving investigational drugs and treatment modalities using FDA-approved drugs. The Investigational Drug Service (IDS) was created in response to the increasing complexity of research protocols and a request by investigators for pharmacy, by virtue of its expertise, to assume the drug management aspects of the trial. Currently, over 50% of the clinical trials managed by the IDS employ investigational anticancer drugs. The IDS coordinates drug procurement, drug storage, inventory control, and drug distribution to the various chemotherapy pharmacies and hospital affiliates. The IDS pharmacist and staff review each investigational chemotherapy protocol from a pharmaceutical viewpoint, create written guidelines for pharmacy personnel, and provide drug information to the nursing staff.
Cancer Support Programs

The University of Chicago Hospitals, “Triumph Over Cancer” program is a cancer support and education program developed to meet the psychosocial needs of cancer patients, survivors, and family members. The program offers several support groups for patients and family members. These programs are available at three locations: University of Chicago Hospitals (UCH), a downtown location, and at Weiss Memorial Hospital, Northside.

These groups are:

- Breast Cancer Support Group
- Prostate Cancer Support Group
- Women’s Cancer Support Group
- General Cancer Support Groups
- Children and Parent Support Groups
- Volunteer (One-on-One Peer Support) Program
- Educational Sessions
- Look Good, Feel Better
- Individual, Family and Marital Counseling
- Information and Community Resources

The University of Chicago Hospitals participate in the National Cancer Survivors Celebration Day. Over 900 cancer patients, survivors and family members participate in a yearly celebration of life. UCH provides entertainment, food booths and a puppet show for children. Speeches by cancer survivors contribute to the cancer support and education program developed to meet the psychosocial needs of cancer patients, survivors, and family members.
Clinical oncology social workers, as integral members of the interdisciplinary health care team, are involved in the identification, assessment, and treatment of oncology patients and their families who have psychosocial and/or environmental needs related to the impact of diagnosis, treatment, hospitalization, and discharge.

The social worker pays attention to the special nuances of the cancer patient’s diagnosis, namely the depression, whether organic or reactive. Counseling focuses around managing the normal feelings of anxiety, sadness, anger, worry, disbelief, depression, and fear of the unknown. Frequently, the social worker must “rehearse” with patients/families alternative outcomes of the illness (namely death). This involves dealing with anticipatory grief and mourning, and where appropriate, making hospice referrals.

Besides providing psychosocial counseling, clinical social workers provide “concrete” services, especially related to discharge planning and continuity of care. These case management services involve referrals for home health care, hospice, homemaker, and transport services.

The major role of the clinical social worker in working with the potential hospice patient is in enabling the patient and family to make the emotional move from one of curative care to palliative care. Patients and families are referred to a variety of hospice programs based upon the geographic location, payor source, and unique psychosocial needs of each case. The majority of patients are referred to VITAS, Horizon Hospice, Hospice of the Calumet Area, Rush Hospice Partners, Palliative Care Center of the North Shore, and Northwestern Hospice.

When a loved one dies from cancer, the grief can be overwhelming for the family. The Hematology/Oncology social workers have recognized this and have created an annual memorial service entitled “Time of Remembrance” to assist families in their mourning. The service is held the first Saturday in May on the atrium level of the Duchossois Center for Advanced Medicine and honors the memory of all cancer patients who had died in the previous year. Two goals of “Time of Remembrance” are to acknowledge the reality of death, human loss and grieving and to assist families in creating closure with the University of Chicago Hospitals and the health care team.

Briefly stated, the clinical oncology social worker is a supportive listener, advocate, mediator, and expeditor for patients/families who are confronting a diagnosis of cancer with all of its uncertainties.
Pastoral Care

Many diseases especially cancer, affects the person’s entire life. That is, body, mind and spirit. It is needless to say that cancer does not only affect the patient and his or her family, but it also affects the caregiver of the patient. The pastoral care giver therefore focuses on the spiritual needs and emotional well being of the patient their family/significant other, and also the teams of care givers.

As the chaplain of Oncology, I work with the multidisciplinary team for the holistic care of the patients. What I do specifically includes assessing the spiritual and emotional needs directly from patients or their families and from referrals from other team members. I give relevant spiritual or emotional support by listening, counseling, reading scriptures, and praying with the patient/ family. Some needs may include administering Sacraments such as communion anointing and baptism. I also refer patients and their families to the on- call chaplains who are on page twenty-four- hours a day, seven days a week. I encourage patients and families to tap the spiritual resources from their faith traditions at home and the community.

On a typical day, I find out from unit nurses and or physicians in rounds who they think would benefit from a chaplain’s visit. Patients and their families are made aware on a daily basis of the available emotional/spiritual support provided by chaplains in any form relevant to their tradition and comfort. Some of the needs addressed include finding peace in an anxious moment such as starting chemotherapy for the first time. Using creative imagery patients are helped to see and accept the ‘chemo’ as a battalion for re-enforcement to fight the cancerous cells. Sometimes we talk about end of life issues such as withdrawal of life support or what death means.

One lady who had battled against cancer for six years said she felt so afraid to die. She perceived death as falling into a bottomless vacuum. After our reflection on her faith tradition she felt comfortable to face her own death and started writing her dreams about her next world.

Many patients find profound strength and meaning in their own life stories when they are encouraged to tell them. What is incredible about this story telling and reflection is that the patients are able to look back and express their gratitude to people who have been there for them and thank their God for their lives.

More often than not I find inspiration from their stories and I am challenged to focus on more important things in life. I also see everyday as a special gift to be appreciated. One of the best parts of working with oncology patients is the bonding, which occurs over long period of time between patients, families and staff. Patients are welcomed back to the unit when they return for continuation of treatment. When death occurs, a special time of remembrance, celebrated by the unit helps families and staff brings closure to a life well lived.

Many cancer patients tend to accept the terminal nature of life in general and so they save their energies to do what is most important to them. For instance building relations with their object of worship and people in their lives.

The chaplain has the privilege of bringing a calming presence of the divine to the holy places of the patients, and listening to the silent healing and joys of life even in the midst of suffering and pain.

Hope beyond life is what many cancer patients teach humankind. The chaplain can be seen as a companion, and I am honored to hold the hands of the suffering and dying as they journey to the next world with hope and meaning.
Exercise training in patients with cancer is safe and effective in improving physiologic and functional status. Physical therapists treat these patients in acute hospital settings to help the patient achieve functional goals, such as bed mobility, transfers, activities of daily living (ADLs) and ambulation. In outpatient and home care settings these patients are encourage to participate in regular exercise programs based on an individual exercise prescription. The exercise training must be individualized for each patient, as the response to exercise will differ between patients, depending on their disease progression.

At the University of Chicago Hospitals, physical therapists treat adult and pediatric oncology in and outpatients. Physical therapy is a part of an interdisciplinary team of patient caregivers. The physical therapist provides an assessment for appropriate assistive devices, special equipment or home modification and to facilitate the transfer from the hospital to the home or rehabilitation center.
Enterostomal Therapy

Enterostomal Therapy (ET) is the specialty that provides care to patients with ostomies, wounds and skin care issues. The ET Clinical Nurse Specialists provide this care in both the inpatient and outpatient arenas. The ostomy patient population includes patients with esphagostomies, gastrostomies, ileostomies, colostomies and urostomies. The rehabilitation of this patient population includes preoperative counseling (preparing for future adjustment, stoma site selection), postoperative instructions (selecting the correct management system, assisting the patient or caregiver to learn management skills), and postdischarge management (problem solving, supportive therapy). Fecal and urinary stomas are generally created as a permanent diversion, and patients require assistance to integrate them into their life style. As patients live with a stoma, their needs may change and a new management system is indicated. The outpatient stoma clinic is available to patients for problem solving and to learn new ostomy management skills.

Gastrostomy tubes can be particularly troubling to patients; when indwelling for a long period of time, leakage can occur making management difficult. The ET nurses can assist in the correct sizing of the tubes, peristomal skin management and patient teaching to reduce the complications associated with the tubes.

The ET nurses can provide consultation regarding prevention as well as intervention protocols. Preventative protocols include pressure reduction and relief surfaces (specialty beds), incontinence skin management techniques, identification of at risk patients and interventions to correct or reduce risk factors, and interventions for treatment of skin breakdown. Interventional protocols include a topical treatment plan of care as well as discharge instructions.

Enterostomal Therapy is a consultative service available by contacting the ET nursing service. This adjunct supportive service contributes to an improved quality of life and cost savings.
ALICIA MATTHEWS, PH.D.
Assistant Professor of Clinical Psychiatry
Director, Behavioral Medicine Service to Oncology

Behavioral Medicine Service

Behavioral Medicine deals with behavioral and psychosocial aspects of medical problems. The Behavioral Medicine Service to Oncology provides psychological assessment and treatment for adults diagnosed with cancer and those at increased risk for the development of cancer. Consultative services are provided to oncology outpatients, family members, and oncology staff members. Diagnostic evaluations focus on social/environmental factors that impact patient’s coping efforts, mood and adjustment. Interventions are aimed at enhancing patient and family coping efforts, treatment of mood disturbance, provision of supportive counseling and psychoeducational instruction to facilitate adjustment. Treatment models include cognitive, behavioral, and interpersonal therapy.

Patients referred to the service are frequently experiencing adjustment reactions and other disturbances of mood and behavior. Common referral problems include depression, anxiety; death and dying concerns, adjustment to treatment side effects (fatigue, pain, nausea, body-image concerns, swallowing difficulty), treatment noncompliance, disease-specific quality-of-life issues, and communication problems between patients, family, and staff. Precipitating circumstances and associated problems typically include a new diagnosis, recurrent cancer, living with cancer as a chronic disease, changes in lifestyle and usual role functions, cancer pain issues, end-of-life concerns, and family/relationship problems. A wide variety of psychological and behavioral interventions are utilized to improve physical and emotional health, self-care, and quality of life. Interventions include: cognitive and behavioral therapy, patient education and skill training, self-management (goal setting, self-monitoring), relaxation, visualization and guided imagery, distraction techniques, assertiveness training, and improving coping mechanisms through identifying antecedents of pain and stress, generating adaptive coping skills, and practicing these skills in actual situations.

The Behavioral Medicine Service to Oncology is also actively engaged in psychosocial oncology research activities. Current studies include:

(1) “Information Seeking Activities of African American Cancer Patients.” This project examines cultural differences in cancer information seeking, treatment decision making, and emotional adjustment following a cancer diagnosis and treatment. The project is funded by the National Cancer Institute.

(2) “Social support, Quality of Life, and Coping in Breast Cancer Patients.” This project explores factors associated with improved outcomes in diverse populations of breast cancer survivors. The project is funded by the Susan G. Komen Foundation.

(3) “Body Image and Sexual Functioning of Breast Cancer Patients.” The objectives of the project are to focus on sexual functioning as a major quality of life concern for breast cancer survivors. Participants with multiple factors that interfere with healthy sexual functioning were hypothesized to report greater sexual dysfunction, poorer adjustment, and relationship difficulties. Further aims of this study were to describe psychological effects, such as anxiety, and explore the relationship between health status, coping behavior, and social support variables on mood disturbance in this population.
Many patients with cancer have nutrition problems requiring the involvement of a dietitian. Nutrition care may improve a patient’s tolerance of cancer therapies and therefore assist in providing an enhanced quality of life. The multitude of side effects that can arise from traditional cancer therapies such as taste changes, nausea and vomiting, and decreased appetite, can cause a significant change in the cancer patient’s nutritional status. To help alleviate some of these difficulties, modifications in diet with close attention to patient food preferences and aversions are essential for improving nutritional status.

In patients with lung cancer some studies have identified associations between total fat intake and incidence of lung cancer. It is likely that dietary fat stimulates cancer growth and acts as a cancer promoter after the initial mutagenic steps have taken place. Adversely, a plant-based diet especially high in fruits and vegetables has been associated with a decreased risk in lung cancer.

Nutritional problems that can occur due to the site of the lung cancer include dysphagia secondary to esophageal compression and difficulty eating secondary to dyspnea. Treatment effects of chemotherapy and radiation include nausea, vomiting, stomatitis, dysgeusia and esophagitis. These nutritional problems caused due to this cancer and its treatment can be dealt with using nutrition therapy, promoting the quality of life and may allow treatment to be more effective.

At the University of Chicago Hospitals, medical nutrition therapy is an integral part of patient care on the Oncology Service. Registered dietitians and dietetic technicians in the department of Nutrition Services strive to meet the specialized nutritional needs of patients with cancer. Dietetic technicians screen new hospital admissions to identify those with current or potential nutrition problems, and monitor tolerance and acceptance of oral feedings and nutritional supplements. Registered dietitians assess nutritional status of patients identified as being at nutritional risk and develop individualized plans of nutritional care. The assessment addresses an individual’s nutritional status, evaluates nutrient requirements, and identifies aspects of the patient’s diagnosis and treatment that could alter nutritional status. The nutritional care plan might include a modified diet, nutritional supplements, education, or enteral/parenteral therapy. Dietitians and diet technicians monitor and adjust, as needed, the nutrition plan of care with any therapy throughout the patient’s stay. Dietitians within the hospital are also available on a consult basis to provide services to patients in the oncology clinic.
Patients who are diagnosed with cancer have several needs. As soon as the patient is diagnosed to have cancer, several aspects of care come to mind. Initial care includes surgery for complete excision of the lesion. This is followed by therapy directed to the cancer cells—chemotherapy and radiation therapy if needed. These patients also need supportive therapy directed to their different specific symptoms related to above.

Pain can be the result of:

1. the rapid multiplication of cancer cells in an organ due to capsular stretch,
2. due to extrinsic pressure on nerves or surrounding viscera,
3. post surgical, related to specific cancer therapy or
4. other causes unrelated to cancer.

Pain management is one of the aspects of the multidisciplinary approach to the patient with cancer. It is directed to the specific needs of each patient based on the specific cause of pain. Major goals of pain management are to treat pain, help preserve quality of life, and minimize side effects.

Since 1994 the agency for Health care policy and research (ACHPR) of the United States department of health and human services has issued special national clinical practice guidelines for the management of cancer pain. These guidelines establish a hierarchy of pain management interventions in which oral and trans-dermal analgesic drugs are the foundations of pharmacologic therapy. This is followed by antineoplastic drugs, Palliative radiotherapy and adjuvant analgesic drugs concurrent with physical and psychosocial modalities where appropriate. The guidelines emphasize that the use of analgesics in pain management must always occur in the context of comprehensive assessment and multimodality treatment.

World Health Organization (WHO) provides a framework for the rational use of oral medication to effectively treat pain of increasing magnitude. Opioid therapy is considered the main stay approach for patients with moderate or severe pain. The basic principles of analgesic use pertain to children as well as adults.
At the University of Chicago’s Pain management center oral therapy is always initiated with non-opioids as tablets, capsules, elixirs & long acting preparations. Patients are encouraged to take medicines on around the clock basis as opposed to as needed (PRN) basis. Weak opioid analgesics and adjuvant drugs are used to treat side effects if needed.

Trans-dermal narcotics are utilized early in patients with bowel obstruction and concerns for poor oral absorption. Judicious use of trans-mucosal opioids can be quite effective in patients with mucositis & stomatitis and in-patients with “event pain” like dressing change. These patients also benefit by administration of opioids via PCA (patient controlled analgesia)

Pain management staff manages pain in house as well as in the pain clinic to maintain continuity of care. Patients are sometimes temporarily hospitalized to optimize medication doses using PCA as a tool. Patients may get continuous intravenous opioids via PCA at home, this initiated by the pain management team can be further managed by home care team. PCA adjusts for variations in response to therapy that result from inter-patient differences in pharmacokinetics and pharmacodynamics. It also allows patients considerable control over the experience of pain.

Intra-spinal administration of opioids has been used to control pain following a variety of surgical procedures and in cancer pain. By binding to spinal cord opioid receptors at the level of injection, intra-spinal opioid administration can produce analgesia at doses that if applied systemically will have a small and transient effect. Due to direct administration of spinal opioids one experiences lower incidence of sedation and nausea. Long term use of intra-spinal opioids has been advocated for cancer pain. Many pain management specialists now believe that selected patients, who are very sensitive to opioid side effects, may benefit from early administration of intra-spinal opioid infusions. These can be infused via fully implanted systems or percutaneous tunneled catheters. External catheters may have risk of infection, which is decreased by fully implanted systems.

Specific nerve blocks, neuro-ablative procedures are done when indicated. Adjuvant drugs like tricyclic antidepressants, antihistamines, Gabapentin, benzodiazepines Clonidine are helpful in neuropathic pain. Steroids can ameliorate painful nerve or cord compression from cancer.

The pain management team provides pain consultations on a 24-hour basis. Patients receive care from board certified pain management specialists on an inpatient or outpatient basis. The center is always eager to optimize care to the patients while minimizing the cost of the therapy. The center is always exploring the use of new and innovative treatments in Pain Management.
MICHELE KUHN
Director, Patient Safety

Patient Safety

In 2000, the Quality and Risk Management staff merged to form the Patient Safety Department of the University of Chicago Hospitals. The goal of the merger was to improve overall performance, and improve patient care in the Hospitals through the identification of close calls and the development of performance improvement projects. In addition, quality indicators used for the Cancer Center include patient satisfaction surveys, the JCAHO ORYX indicators and the patient safety reports.

Chemotherapy Order Documentation Compliance

The Chemotherapy Performance Improvement Team (CPIT) formed in 1995. CPIT continues to meet and proposes improvements for prescribing, dispensing, and administration of chemotherapy drugs. In 2001, UCH revised the policy aimed at ensuring safe administration of chemotherapy to our patients.

Time Period of Review:
Each quarter, medical records, for adult/pediatric inpatient and outpatient chemotherapy, are reviewed on a rotating basis.

Benchmark:
UCH has an institutional goal of 100% compliance with all key documentation related to chemotherapy administration.

Results:
Currently, UCH demonstrates an overall documentation compliance rate of 95%. Analysis of data showed that the major areas in need of performance improvement include patient’s name on each page of chemotherapy order, and nurse and physician documentation of patient’s psychosocial response.

Follow-up:
UCH will continue to audit chemotherapy orders to ensure that the correct documentation is taking place. UCH policy requires that if compliance falls under 100%, the CPIT will develop a corrective action plan to increase compliance.

Goal:
The current goal of the CPIT Committee is to combine chemotherapy notes and orders. This will help eliminate the risk of errors in transcription and eliminate duplication of paperwork.
PAIN ASSESSMENT FOR CHEMOTHERAPY PATIENTS

Appropriate pain control fosters patient comfort, facilitates healing and enhances satisfaction. In response to the issues identified by the Pain Management Taskforce, the Chemotherapy Performance Improvement Team (CPIT) incorporated assessment of pain into their audits.

**Time Period of Review:**
Each quarter, medical records, for adult/pediatric inpatient and outpatient chemotherapy, are reviewed on a rotating basis.

**Benchmark:**
The performance target is for all patients to be screened for pain upon admission to the hospital and to be reassessed for continuing pain or new onset of pain during the hospital stay. Additionally, all outpatients are to be screened for pain prior to beginning treatment and again after treatment is completed.

**Results:**
The study found that 98% of inpatients were screened for pain during their admission and 100% had a pain assessment on each shift. Additionally, 100% of all outpatients were screened for pain at the time of their treatment and again prior to discharge.

**Follow-up:**
Pain assessment will continue to be monitored as part of the chemotherapy compliance audits.

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**Pain Management Quality Improvement Project**

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<td>Q3 = Was patient screened for pain for each outpatient encounter?</td>
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<td>Q4 = Was patient screened for pain for each outpatient encounter prior to discharge?</td>
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Cancer Registry

The Cancer Registry Department at the University of Chicago Hospitals plays an active role in the cancer program by providing multiple services and support for the components of a Commission on Cancer (CoC) approved cancer program. The cancer registry coordinates the collection, research, management, analysis and dissemination of cancer information.

Since 1946, we have collected and maintained over 75,000 cancer cases and over 2,300 new cases are entered each year. Of these 2,300 cases 72% were analytical, meaning the patient was diagnosed and/or received their first course of treatment at the University of Chicago Hospitals. Non-analytical cases, those patients that were diagnosed and/or received their first course of treatment at a different facility and were referred to the University of Chicago Hospitals for a recurrence or subsequent treatment, represent the remaining 28% of the total cases.

Each new case involves collecting over 100 data items including patient demographics, diagnosis, cancer treatment, disease staging, and lifetime follow-up. The registry works diligently to follow the specific requirements set by the American College of Surgeons, Commission on Cancer, and the Illinois State Cancer Registry.

A Few of the Accomplishments during 2002 include the following:

- Abstracted over 2,300 cases
- Quality Control of registry data was performed on 10% of analytical cases
- Submitted data to the Illinois State Cancer Registry on all 2002 accessioned cases as mandated
- Initiated follow-up on a monthly basis with over 10,000 patients currently being followed, while maintaining a follow-up rate of 90%
- Casefinding study from the Illinois State Cancer Registry Quality Control Program, achieving 100% compliance
- Submitted requested data to the National Cancer Data Base

The data in the registry database is utilized in many ways and the use of the information is encouraged by the University of Chicago Hospitals.
## Incidence by Primary Cancer Site – 2002 (Site Analysis)

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<td>III – Defined &amp; Unspecified Sites</td>
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**TOTAL** 2387 1726 661

Analytic: Cases diagnosed and/or received first course of treatment at UCH.

Non-Analytic: Cases diagnosed and received first course of treatment elsewhere.

*Excludes localized basal and squamous cell carcinomas of the skin

**Excludes carcinoma “in-situ” of cervix
Five Most Common Sites By Percentage

- **Colon Cancer**
  - Stage 1: 40%
  - Stage 2: 35%
  - Stage 3: 30%
  - Stage 4: 25%
  - Unknown/NA: 15%

- **Corpus Uteri**
  - Stage 1: 50%
  - Stage 2: 45%
  - Stage 3: 40%
  - Stage 4: 35%
  - Unknown/NA: 30%

- **Lung Cancer**
  - Stage 1: 35%
  - Stage 2: 30%
  - Stage 3: 25%
  - Stage 4: 20%
  - Unknown/NA: 10%

- **Breast Cancer**
  - Stage 0: 35%
  - Stage 1: 30%
  - Stage 2: 25%
  - Stage 3: 20%
  - Stage 4: 15%

- **Prostate Cancer**
  - Stage 1: 80%
  - Stage 2: 70%
  - Stage 3: 60%
  - Stage 4: 50%
  - Unknown/NA: 40%
Comparison of UCH, Illinois and National Percentages

Lung Cancer # of Cases Accessioned Each Year

All Cancer Cases # of Cases Accessioned Each Year
Lung Cancer, Observed Survival Analysis (UCH vs. NCDB)

### Stage 1
- Years: 0, 1, 2, 3, 4, 5
- NCDB 94-95
- UCH 94-95

### Stage 2
- Years: 0, 1, 2, 3, 4, 5
- NCDB 94-95
- UCH 94-95

### Stage 3
- Years: 0, 1, 2, 3, 4, 5
- NCDB 94-95
- UCH 94-95

### Stage 4
- Years: 0, 1, 2, 3, 4, 5
- NCDB 94-95
- UCH 94-95
SITE SUMMARY

At the University of Chicago Hospitals we offer a variety of different services to meet the physical and emotional needs of every patient. We understand that each patient is unique. Our goal is to provide the best care and services that we can offer.

In 2002, the American Cancer Society (ACS) predicted approximately 1,284,900 new cancer cases in the United States. Of these cases, approximately 169,400 cases are expected to present as lung cancers. Lung cancers account for roughly 2% of new cancer diagnoses.

Of the 2,387 total cancer cases seen at the University of Chicago Hospitals in 2002, 233 cases were diagnosed and/or treated for lung cancer. Lung cancer represents 10% of the cases seen at the University of Chicago Hospitals. Of these, in 2002, 26% received surgery followed by 18% of the patients who received chemotherapy alone, as illustrated in the graphs below, and all cases are routinely discussed at the multidisciplinary, weekly, Tumor Board Conference.

Lung cancer can significantly alter a patient’s quantity and quality of life. In fact, according to the American Lung Association, it is the leading cancer killer in the United States; therefore, prevention, early diagnosis, and effective treatment are crucial components of any comprehensive approach.

Any cancer can become deadly if left untreated. The cancer committee works diligently to increase awareness and involvement of all physicians to improve our cancer program.

Lung Cancer, First Course of Treatment Analytic Cases

All Cancer, First Course of Treatment Analytic Cases
ABOUT US

HISTORY AND MISSION

Established in 1973, The University of Chicago Cancer Research Center (UCCRC) is one of 61 nationally designated Clinical Cancer Centers by the National Cancer Institute. This prestigious designation is awarded to cancer centers that have strong research programs in basic and clinical sciences. These programs must be fully integrated through productive collaborations between cancer center members. The UCCRC conducts innovative clinical trials, and provides cancer education and outreach to the surrounding community. An NCI designated cancer center must make significant contributions to advances in cancer research that are key to understanding, preventing, and treating this disease. Such a distinction is a reflection of our dedication to eliminating cancer through laboratory research, innovative clinical trials, and prevention research.

Our 175 members represent 16 departments throughout the University and include internationally recognized basic scientists and clinicians. All members participate in six established research programs and interact through fruitful collaborations. These programs include:

- Cell Signaling and Gene Regulation
- Molecular Genetics and Hematopoesis
- Immunology and Cancer
- Clinical and Experimental Therapeutics
- Advanced Imaging
- Clinical Cancer Genetics and Prevention

On the clinical side, the UCCRC is a leader in the development of novel agents for cancer treatment. Major areas of clinical research include leukemia, breast cancer, new drug development, simultaneous head and neck cancer, lung cancer, kidney cancer, prostate cancer, mesothelioma, and cancer genetics.

Our equally strong basic science programs have pioneered studies in the molecular genetics of hematologic cancers (leukemias, lymphomas), cancer immunology, cell signaling, and advanced imaging techniques.

Cancer prevention research at the UCCRC focuses on identifying genetic risk factors for cancer, investigating potential chemoprevention agents, early detection, and quality of life issues.

The UCCRC supports the following core laboratories that provide cutting-edge technology for our members’ research projects. They include:

**DNA Sequencing Facility**
- Oligopeptide Synthesis Facility

**Immunology Applications**
- Human Immunologic Monitoring Facility

**Digital Light Microscopy Facility**
- Electron Microscopy Facility
- Magnetic Resonance Imaging and Spectroscopy Facility
- Scientific Visualization and Image Analysis Facility
- Transgenic Mouse/Embryonic Stem Cell Facility

**Laser Capture Microdissection Facility**

**Pharmacology Core Facility**
- Biostatistics Consulting Lab
- Cancer Clinical Trials Office (formerly Protocol and Data Management Office)

**Functional Genomics Facility**

**cGMP Facility**
OUR MISSION

- to stimulate and support collaborative interdisciplinary laboratory research in cancer;
- to advance discoveries and new treatment strategies from the laboratory to clinical application;
- to apply modern techniques of molecular biology, genetics and cytogenetics to the study of human tumors;
- to conduct multidisciplinary clinical treatment programs for patients with cancer;
- to provide education and training in cancer research for basic scientists, clinical investigators and health care professionals at all levels of training;
- to provide access to clinical trials to community oncologists and minority populations via a network of affiliated hospitals and
- to initiate and develop cancer prevention and control research at the University of Chicago and the Chicago metropolitan area.

The UCCRC is the sole supporter of the Cancer Resource Center, which is located in the Duchossois Center for Advanced Medicine and provides guidelines for the early detection and prevention of various forms of cancer, as well as information about treatment and support services for patients.

UCCRC

1966
Charles B. Huggins M.D. awarded Nobel Prize for his work on the hormonal control of breast and prostate cancers

1998
Janet D. Rowley, M.D. awarded National Medal of Science for her discovery of chromosomal breakpoints and their role in cancer.
FACTS AND FIGURES

University of Chicago Cancer Research Highlights

An innovative multi-disciplinary cancer program, the University of Chicago is internationally recognized as a center for the diagnosis and treatment of malignant disease and has a special expertise in leukemia, as well as cancers of the head, neck, breast, bowel and prostate.

The University of Chicago ranks among the premier institutions in the United States for cancer research and clinical care. Its Cancer Program was ranked 6th by U.S. News and World Report in 2003. The University of Chicago Cancer Research Center is the top dollar recipient of NCI funds in the state.

Clinical research has always been a vital component of the Cancer Center, and it continues to thrive today. During 2000, cancer patients accounted for 62,209 outpatient visits and 2,758 inpatient admissions. Enrollment of patients on clinical research protocols has increased dramatically in recent years from approximately 250 annually in 1988 to 1,690 in 1999.

DNA testing for familial cancer is gaining recognition as a critical tool for cancer prevention. Publicity about this new development has almost doubled the referrals to the Cancer Risk Clinic, the only fully operational clinic in Illinois providing genetic services to patients with a family history or genetic predisposition to cancer.

The University of Chicago has become a national center for bone marrow transplantation and for research into this promising technology. Chicago’s bone marrow transplantation program attracts patients from across the United States and is currently one of a handful of institutions providing autologous bone marrow transplantation.

The Children’s Hospital is one of the first institutions to offer a particularly exciting development in the treatment of leukemia — the use of placental blood as a source of “stem cells” for transplantation. Until this technology, bone marrow transplantation had been the “last resort” treatment for pediatric leukemia — and a difficult treatment option, since it had been dependent upon finding a “perfectly-matched” donor.

The University of Chicago’s Ben May Institute for Cancer Research provides unique support to cancer research and the application of research advances to the diagnosis and treatment of the disease. Ben May Institute scientists make contributions to our understanding of cell growth, differentiation and replication and to the development of therapies involving hormones, growth factors and specialized monoclonal antibodies.
In 1943, Dr. Leon O. Jacobson and his colleagues were among the first to develop a specific cancer chemotherapeutic agent, nitrogen mustard. That same year, scientists at the University pioneered the concept of total body irradiation.

Clinical work and fundamental research culminated in the discovery of a hormonal therapy for prostate cancer, a discovery that earned the late Dr. Charles B. Huggins the 1966 Nobel Prize for Physiology and Medicine. In all, 11 of the 75 University of Chicago Nobel laureates were affiliated with the Medical Center.

During a career that spanned more than 35 years, Dr. Elwood Jensen, the Charles B. Huggins Distinguished Service Professor, developed procedures to predict whether patients with breast cancer would benefit from hormonal therapy.

In 1973, Dr. Janet Rowley, the Blum-Riese Distinguished Service Professor of Medicine, identified a genetic translocation in patients suffering from a cancer of the blood called chronic myelogenous leukemia. This insight proved central to our understanding of the relationships between genetics and malignancy, and initiated a flurry of discoveries concerning other types of leukemias and lymphomas. Dr. Rowley was recently recognized for her breakthrough work with the 1998 Lasker Award. She was also one of eight researchers who was awarded the National Medal of Science by President Clinton.

Some of the most recent discoveries include that of Dr. Ralph Weichselbaum who identified specific cancer cells that resist radiation therapy in head and neck tumors. This insight has already improved diagnosis and therapy planning.
MARK K. FERGUSON, M.D.
Professor, Cardiac & Thoracic Surgery

The Role of the Surgeon in Diagnosing and Treating Lung Cancer

Since the first successful resections were performed for lung cancer 75 years ago, substantial progress has been made in the surgical management of lung cancer. As a result, despite numerous advances in our understanding of the pathobiology of this disease and the resultant development of therapies, surgery remains one of the mainstays of curative therapy for lung cancer.

Techniques such as flexible fiberoptic bronchoscopy and sputum cytology remain the basic tools for lung cancer diagnosis. Advances in radiology have led to the introduction of low dose helical computed tomography for screening for lung cancer, which is effective in identifying small lung nodules not evident on plain chest radiographs. Such nodules are not amenable to bronchoscopic biopsy, percutaneous aspiration for cytology, or further characterization by PET scanning. As a result, the identification of a small peripheral nodule often requires the input of surgeons for diagnostic assistance. Thoracoscopic biopsy techniques, sometimes directed by fluoroscopic identification of radiopaque markers placed under CT guidance, offer the ability to diagnose and treat some such early stage cancers. The benefit and cost-effectiveness of this technique are currently under investigation.

An additional new screening measure that is being introduced in some medical centers is LIFE (light-induced fluorescence endoscopy) bronchoscopy. This technique relies on excitation of natural autofluorescence in precancerous or cancerous tissues by specific wavelengths of light. It permits detection of carcinoma-in-situ or early stage cancers in patients who are at high risk for new cancer development after successful treatment of early stage lung cancer.

Minimally invasive techniques are being used with increasing frequency for lung cancer diagnosis and staging. The recent introduction of endoscopic ultrasonography for biopsying mediastinal lymph nodes complements the use of transbronchial biopsy and thoracoscopy. Mediastinoscopy continues to be a mainstay of mediastinal staging for lung cancer owing to its ability to assess mediastinal tumor invasion as well as reliably stage individual lymph node stations.

Surgery continues to be the best initial treatment for early stage (I, II) non-small cell lung cancers (NSCLC). Standard therapy is lobectomy, with lesser resections (wedge resection, segmentectomy) reserved for patients with limited pulmonary reserve or co-morbid factors that increase the risk of major lung resection. Pneumonectomy is avoided whenever possible owing to the increased risk of the operation and its long-term detrimental effects on quality of life and possibly on survival. Minimally invasive techniques are being investigated for their role in resection of early stage lung cancer; no definite benefit has yet been established. Recent information suggests that all resected NSCLC patients except those in the earliest disease stage (Ia) benefit from postoperative adjuvant therapy. These findings have important implications for ongoing studies of neoadjuvant chemotherapy for such patients.

The role of resection for patients with more advanced stages of disease is controversial. Recent information suggests that patients who have microscopic single mediastinal nodal station involvement do well after initial resection. However, the accurate identification of this subset of patients prior to resection is problematic. Patients with known ipsilateral mediastinal nodal involvement undergo neoadjuvant chemotherapy and possibly radiation therapy; patients who do not experience tumor progression are recommended to undergo resection.

Patients with NSCLC associated with contralateral mediastinal adenopathy, malignant pleural effusion, or distant metastases generally are not candidates for surgical intervention except to palliate symptoms related to their disease. This is particularly true for symptoms of dyspnea related to airway obstruction or pleural effusion. The exception to this guideline is the presence of oligometastatic disease, especially an isolated brain metastasis, in the presence of otherwise early stage disease. In such rare instances formal lung resection may be considered if the metastatic disease is eradicated.
The Role of the Medical Oncologist in the Treatment of Lung Cancer

The treatment of lung cancer is a multidisciplinary effort, involving thoracic surgery, radiation oncology and medical oncology in formulating a treatment plan for each patient. Although the medical oncologist consults on many different aspects of lung cancer treatment, the major treatment modality used is chemotherapy, which is playing an increasingly significant role in lung cancer management. Newer chemotherapy drugs that have activity in lung cancer include paclitaxel, docetaxel, gemcitabine, vinorelbine and irinotecan. In general, they are more active against the cancer than older drugs, and are also generally better tolerated in terms of short-term side effects.

Patients with small cell lung cancer, who represent about 20% of all patients with lung cancer, are routinely treated with combination chemotherapy. Chemotherapy has been the mainstay of treatment for small cell cancer for 30 years. Tumor response rates are very high, including frequent complete remissions. Patients often feel significantly improved after only a few weeks of treatment. A small percentage of patients with limited-stage small cell cancer appear to have long-term remissions, lasting more than 5 years.

Chemotherapy has been playing an increasing role in the management of non-small cell cancer. Patients with advanced disease are typically treated with platinum-based chemotherapy. Response rates are around 40%, with an additional 30-40% of patients having stable disease for a period of time. A high percentage of patients will have relief of one or more of their major symptoms with chemotherapy. Patients with stage III disease, or locally advanced lung cancer, are now routinely treated with chemotherapy along with radiation therapy, as the combination, particularly when given concomitantly, appears to afford better and longer remissions than radiation alone.

At the recent meeting of the American Society of Clinical Oncology, a major trial was reported using postoperative adjuvant chemotherapy for earlier-stage patients after their initial surgery. The trial was a positive one, leading to about 5% increase in 5-year survivals in favor of the patients who received chemotherapy. Accordingly, we are offering adjuvant chemotherapy to more patients in this setting.

The major realm of research currently in advanced lung cancer is in the use of small targeted molecules, which aim to disable the cancer cell by honing in on a particular step in its growth. There is also interest in anti-angiogenesis (inhibiting blood vessel formation by the tumor) drugs. Both of these types of drugs are given in conjunction with chemotherapy drugs in a number of our clinical trials. One drug that was recently approved by the FDA for treatment of refractory lung cancer is gefitinib (Iressa). This is a well-tolerated drug which is a small targeted molecule. Although response rates are not high to gefitinib, some patients respond very dramatically, and can feel considerably better.

Although progress has certainly been made, considerable improvement is still needed in the chemotherapy management of lung cancer. We have an active Phase II clinical trials network, as well as a Phase I contract to test new drugs. This allows us to have drugs available to offer patients who sometimes have little hope of benefit from existing drugs. While many of these investigational drugs do not ultimately prove beneficial, all of the drugs currently on the market were once in a testing phase, and therefore some will turn out to be active in a variety of tested cancers. These clinical research efforts continue in hopes of improving our fight against lung cancer.
The role of the radiation oncologist in treating lung cancer can take many forms. The precise role depends on the stage of disease, histology of the cancer, and condition of the patient. In some patients the role is to administer potentially curative therapy. In others the role may be to palliate symptoms and address quality of life issues. There are situations when the radiation oncologist will act alone in treating the patient. Frequently the role of the radiation oncologist will be as part of a multidisciplinary team treating the cancer.

The role of the radiation oncologist is limited in most patients with early stage (Stage I and II) non-small cell lung cancer (NSCLC). Most of these patients are better served by surgical resection of the tumor. However, not all patients are medically fit for a major surgery. In those patients with early stage disease who are technically resectable but medically inoperable, the role of the radiation oncologist is to administer radiation therapy with curative intent.

Some patients with NSCLC may present with what seems to be early stage disease but are found to have more advanced (Stage IIIa or IIIb) disease at the time of surgery. These patients are at high risk of local and distant failure. In this situation role of the radiation oncologist is to administer adjuvant radiation to the mediastinum and draining lymph nodes to reduce the chances of a local failure. The radiation is often delivered in conjunction with chemotherapy as part of a combined modality approach to address the potential for distant failure as well.

Those patients presenting with locally advanced (Stage IIIa and IIIb) NSCLC are frequently considered unresectable. Most of these patients receive combined modality therapy consisting of radiation and chemotherapy. The role of the radiation oncologist is to deliver potentially lethal doses of radiation to the primary tumor and involved lymph nodes while sparing as much normal tissue as possible. The chemotherapeutic agents given with radiation tend to enhance the effectiveness of radiation while addressing the potential of distant metastatic disease.

The radiation oncologist has played a major role in the treatment of small cell lung cancer. Unlike NSCLC, patients with small cell lung cancer are not usually considered to be surgical candidates due to the high risk of occult distant metastases. The integral role of radiation in this lung cancer histology is reflected in a commonly used staging system that divides patients into two groups (limited and extensive disease). This division is based on the determination of the radiation oncologist. Patients are considered to have limited disease if the gross tumor can be encompassed in a single radiation port. The standard treatment for patients with limited stage small cell lung cancer is radiation with concomitant chemotherapy.

Patients with limited stage small cell lung cancer achieving a complete response to treatment have a high risk of developing brain metastases as the first and often the only site of failure. In this situation the role of the radiation oncologist is to administer prophylactic cranial radiation. By treating the brain with a brief course of low dose radiation, many of these metastases can be prevented.

Patients with lung cancer often present with or develop metastatic (stage IV) disease. Metastatic lesions in the bone can result in pain or weaken the bone over time running the risk of pathologic fracture. Radiation therapy has been and remains the standard treatment in these situations. A short intense course of radiation will decrease or eliminate the pain resulting for bone metastases in 80% of patients. A similar course of radiation will reduce the risk of a pathologic fracture in a weight bearing bone.

Other patients with lung cancer may develop neurological symptoms when they develop brain metastases or when the tumor encroaches upon the spinal cord. Most of these patients are referred for radiation treatment. In these cases radiation therapy can stabilize or reverse the symptoms patients experience.

In summary, the radiation oncologist has multiple important roles in the treatment of lung cancer. These roles vary depending on the stage and histology of the lung cancer. Radiation may be used: 1) as a single modality with curative intent; 2) as part of a combined curative intent treatment with chemotherapy; 3) to palliate symptoms in patients with advanced cancer.
LIVIA SZETO, RN, BSN

The Role of Nursing in Lung Cancer

Nursing care can be very challenging when a patient is diagnosed with lung cancer. The majority of lung cancer patients present with an advanced stage at the time of their diagnosis. Median survival is only 7 to 12 months. Patients and family need a lot of support, education and prompt care.

Smoking is one of the biggest risk factor in lung cancer, patients who smoke, sometimes get labeled as “you’re the one to blame for your lung cancer” from family and friends. For the second-hand smoker patients, usually it is their significant ones who are the smokers; they feel guilty, because they cause the cancer for the love one. Emotional support is very crucial for patients and family. Guilt, shock and denial are often the emotions that nurses encounter when meeting lung cancer patient for the first time. The role of listener is what nurses do best at this encounter.

We are the key people to support and educate patients and family about their diagnosis and treatment of lung cancer. We make referrals to social work department, behavioral medicine division, and nutritional service, home care service when applicable.

Since lung cancer treatment does not have a very good cure rate in advanced stages, it is very important to teach patients and family that the planned treatment may not be a cure. The goal is to relieve symptoms and to improve or maintain their quality of life. When treatment is no longer feasible; we will initiate hospice care.

The lung cancer research nurse role is to identify, screen and enroll patients onto clinical trials. We monitor, intervene and report side effects of the treatment. We act as a liaison for the multidisciplinary teams, patients, oncologist, radiation oncologist, and surgeons. We coordinate treatment plan and facilitate communication within the team. This is all done in an effort to give the best care to patients and their families.
# TUMOR BOARD CONFERENCE SCHEDULE

<table>
<thead>
<tr>
<th>Day/Conference</th>
<th>Physicians</th>
<th>Time</th>
<th>Location</th>
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</thead>
<tbody>
<tr>
<td><strong>Monday</strong></td>
<td></td>
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<tr>
<td>Hematology/Oncology</td>
<td>All Hem/Onc Faculty</td>
<td>11:30 a.m.</td>
<td>E215</td>
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<tr>
<td><strong>Tuesday</strong></td>
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<tr>
<td>Genitourinary Oncology</td>
<td>Jani/Sokoloff/Stadler/Vogelzang/Zimmerman</td>
<td>8:00 a.m.</td>
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<td>Head and Neck</td>
<td>Baird/Gustin/Haraf/Mauer/Recant/Stenson/Vokes</td>
<td>8:00 a.m.</td>
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<tr>
<td>Pediatric Oncology</td>
<td>Beyer/Husain/Rubin</td>
<td>10:00 a.m.</td>
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</tr>
<tr>
<td>Gastrointestinal Oncology</td>
<td>Hart/Kindler/Michelassi/Posner</td>
<td>12:00 p.m.</td>
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</tr>
<tr>
<td>Leukemia</td>
<td>Larson/Odenike/Smith/Stock</td>
<td>1:00 p.m.</td>
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<td>Neurology Tumor</td>
<td>Hekmatpanah</td>
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<td>Bone and Soft Tissue</td>
<td>Gajewski/Montag/Peabody/Simon</td>
<td>4:00 p.m.</td>
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<td>Chest/Esophageal</td>
<td>Abrahams/Ferguson/Haraf/Hoffman/Husain/Mauer/Rudin/Vokes</td>
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<td>Mesothelioma</td>
<td>Armato/Husain/KindlerRaman/Vogelzang</td>
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<td>Gynecologic Oncology</td>
<td>Fleming/Herbst/MontagRottmensch/Yamada</td>
<td>9:00 a.m.</td>
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<td>Phase I</td>
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<td><strong>Thursday</strong></td>
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<td>Breast</td>
<td>Chaekal/Chhablani/Conzen/Fleming/Hoffman/Jaskowiak/Mauer/McKee/OlopadeRecant</td>
<td>8:30 a.m.</td>
<td>G217</td>
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<tr>
<td>Marrow Transplant</td>
<td>Larson/Odenike/Stock/VanBesien/Zimmerman</td>
<td>9:00 a.m.</td>
<td>E215</td>
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<td>Surgical Oncology</td>
<td>Posner/Jaskowiak/McKee</td>
<td>4:00 p.m.</td>
<td>G217</td>
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</table>
The next time you need a physician-to-physician consult, call Physicians’ Access Services, the Medical Center’s toll-free hotline for referring physicians. Staffed seven days a week, 24 hours a day by specialists trained to expedite your calls, Physicians’ Access Services gives you immediate access to specialists in virtually every subspecialty area. They will assist you by connecting you with the appropriate expert for your needs. And, these experts are committed to keeping the referring physician involved in the care team. Physicians’ Access Services is one example of our renewed commitment to serving referring physicians. This service will save you time and energy by virtually eliminating multiple transfers, waiting on hold, and other delays.

In addition, you can use Physicians’ Access Services for:

Admission and outpatient appointments. The staff is experienced in coordinating urgent and elective admissions and appointments in our hospitals and clinics.

Patient transfers and transports. The staff will help you coordinate with the attending physician and admission services. Staff specialists may also assist you in arranging transportation to the University of Chicago Hospitals if it is necessary.

Physician to Physician consultations. The next time you need a physician-to-physician consult, call 1-800-UCH-2282 for assistance during every stage of patient care, from diagnosis to discharge to home care.

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UNIVERSITY OF CHICAGO CANCER RESEARCH FOUNDATION
The University of Chicago Cancer Research Foundation is a private, not-for-profit organization that seeks funds to underwrite basic and clinical research programs on the causes and treatments of cancer. Few voluntary efforts require a deeper commitment or offer a more compelling opportunity to have an impact on the health, social and economic welfare of our entire society.
BOARDS AND AUXILIARIES

Auxiliary organizations participate fully in the activities of the University of Chicago Cancer Research Foundation. Their generosity has made possible improved hospital and laboratory facilities, additional equipment, and fellowships for young scientists in cancer research. They help to support the work of some of the University’s most distinguished research scientists. In addition, a number of groups have made unrestricted gifts, providing funds which give scientists essential flexibility and can be used where the need is greatest.

The continued support of the volunteer organizations reflects their dedication to the University’s cancer research activities and their understanding of the problems involved in financing complex medical research programs.

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The Board of Trustees has established the UCCRF Board of Trustees Endowment Fund to support cancer research programs in the Cancer Center.

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The Women’s Board impressive history of funding faculty recruitment and research of the BMICR has been critical to its success. Over the past five years, they have invested in the research of Dr. Kay Macleod, whose work has focused on the transcriptional regulation of tumor suppressor genes and in the research of Dr. John Crispino, a talented young researcher whose work in blood cell development encompasses childhood leukemia. This year, their gift will help to focus our recruitment efforts in the field of the regulation of DNA repair mechanisms, particularly in response to DNA damage from the environment. Additional recruitment of candidates dealing with the study of the mechanisms by which cells respond to external signals and either grow or die through apoptosis (programmed cell death) is in progress. Understanding these mechanisms is important, not only, for our ability to understand fundamental cellular processes, but also, it will enable us to identify key targets for therapeutic treatment of tumors.

Marsha Rosner, Ph.D.
Charles B. Huggins Professor and
Director, Ben May Institute for Cancer Research
Professor, Dept. of Neurobiology, Pharmacology and Physiology and
Committees on Cancer Biology, Cell Physiology and Developmental Biology

The Women’s Board provides funds for:

THE BEN MAY INSTITUTE
FOR CANCER RESEARCH:

[Image of Marsha Rosner]
The Committee, ranked as one of the premier cancer research degree-granting programs in the nation, remains a critical resource for the best future researchers in cancer. Private funding that the Women's Board provides ensures that we continue to attract and educate the most promising students in the world. This year the Women's Board support honored these very fine students:

**CANCER BIOLOGY FELLOWS:**

**Elaine Ehrman Fellows**

This year there were several excellent candidates for the Elaine Ehrman Award. Two stood out as being extraordinary making it difficult to select one over the other. For this reason two Elaine Ehrman Fellows were awarded this year as they have both done outstanding work in the area of cancer research.

**Brian Barnhart**

Bryan (Bo) received his B.A. in Biological Sciences from Rutgers College of Rutgers University in May, 1996. Following graduation Bo stayed at Rutgers for three years as a Research Technician in Dr. Lori Covey’s laboratory working in the field of molecular immunology while concurrently earning his teaching certification for secondary biology education. He is currently a fifth year student in the Committee on Immunology at the University of Chicago and works in the laboratory of Dr. Marcus Peter. Bo’s research focuses on analyzing the molecular mechanisms of cell death as it relates to the development of cancer.

**Kendall Nettles**

Kendall received his B.A. in Psychology at Colgate University in May, 1994, after which he worked as a Research Assistant with Dr. Morris B. Goldman in the Department of Psychiatry at the University of Chicago for four years. He is currently a sixth year student in the Committee on Cancer Biology working in the laboratory of Dr. Geoffrey Greene. Kendall’s research focuses on analyzing the atomic details of the estrogen receptor in complex with naturally occurring hormones or anti-cancer drugs such as tamoxifen.

**Continuing Student Fellow for 2003 is Rebecca Conkling**

Rebecca received her B.S. from Binghamton University in May, 2002, entered the Cancer Biology program in the summer of 2002, and is currently working in the laboratory of Dr. Karen Frank. Her research focuses on understanding the DNA repair mechanisms that are mutated during carcinogenesis, specifically the role of several DNA repair proteins that are mutated during tumor formation.

**Continuing Student Fellow for 2003 is Robert Schickel**

Robert received his B.S. in Biochemistry from the University of California, San Diego in June, 2003. He entered the Cancer Biology program in the summer of 2003, and recently did a rotation in Dr. Marcus Peter’s laboratory. His research interests are in the study of signal transduction mechanisms as they relate to tumorigenic growth and invasiveness.
The Women’s Board has played an integral role in supporting research which has led to the discovery of genetic targets in cancer. As a result of this success, University of Chicago cancer investigators are now able to focus on the next steps in that path, namely on the drugs which interfere with those proteins that are altered in tumor cells. Two years ago, the Women’s Board helped to establish a core facility to develop proteomics, the study of proteins. Proteins are truly the engines that drive cancer cells. This year’s funding will advance highly sophisticated proteomics research, by furthering the expansion of proteomics into drug discovery, the “breakthrough” stage of this continuum – the development of effective new compounds that will interact with protein targets to inhibit the growth of cancer.

The UCCRC is a national leader in cancer clinical trials. These trials are a fundamental part of our fight against cancer. With help from Women’s Board funding, the UCCRC has attempted to construct and maintain a comprehensive cancer clinical trial management informatics tool to better manage the diverse and voluminous data generated by both the regulatory and clinical aspects of the many and new cancer trials planned and activated each year in addition to the hundreds already open. The UCCRC AdvanceLink project integrates a diffuse array of clinical, regulatory, and administrative data from clinical trials. It incorporates ancillary data such as grants, contracts, researchers, institutions, publications, staffing resources, audits, clinical samples, quality of life and other correlative research projects into a master centralized database through custom user interface software. This database allows all researchers and their teams to audit, analyze, and report data more effectively and efficiently with strengthened mechanisms for protecting the health information of our patients and their families.
The Clinical Cancer Genetics and Prevention program is a major strength of the UCCRC Cancer Control Population Science effort. The UCCRC is committed to expanding the scope of its cancer control and prevention efforts in a way that complements its basic and clinical research. With the completion of the Human Genome Project, tremendous gains in the knowledge of the structure and function of human genes have lead to more effective cancer control through the use of genetics to quantify individual risks. This year's funding will continue the Cancer Research Center's momentum, towards developing ways to prevent cancer, (i.e., smoking cessation research, prevention of cancer through macronutrients such as raspberry extracts) and to detect it in its earliest stages, (i.e., specialized x-rays and blood tests).

Olufunmilayo I. Olopade, M.D.,
Professor of Medicine, and Director, Center for Clinical Cancer Genetics

The Women's Board has supported the establishment and expansion of this important facility for the last several years. This year's support makes possible the expansion of the current capabilities of this facility into state-of-the-art proteomics research. It will allow the UCCRC to meet the demands of its member investigators to continue to perform state-of-the-art biological research and to maintain our competitive edge among other institutions.

Xinmin Li, Ph.D.,
Senior Research Professional, Department of Medicine/Section of Nephrology
This year’s support allowed the purchase of a microemulsifier, needed to produce perfluorcarbon emulsions. Perfluorcarbon emulsions are used as MR contrast agents for detection and evaluation of cancer. This equipment will provide added advantage to develop improved formulations of perfluorocarbons that will improve our ability in the early detection and staging of cancer.

Greg Karczmar, Ph.D.,
Associate Professor, Department of Radiology, and Director, Magnetic Resonance Imaging and Spectroscopy Laboratory

In 2001, with major support of the Women’s Board, Laser Capture Microdissection (LCM) was brought to the University of Chicago. These techniques allow for microdissection and extraction of cell populations or single cells for further molecular analysis. Microdissection in this facility has been successfully used for accurate molecular analysis of tumors and their precursor lesions. This year’s funding will provide for the purchase of a fluorescence detection upgrade for the system, and will significantly accelerate cancer research projects requiring precise laser microdissection of cancer cells without contamination by adjacent non-cancerous cells.

John Hart, M.D.,
Associate Professor, Department of Pathology
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THE AUXILIARY BOARD PROVIDES FUNDS FOR
THE RESEARCH OF THESE CANCERS SPECIALISTS:

Mark D. McKee, M.D.

As an Assistant Professor in the Department of Surgery at the University of Chicago, Dr. McKee’s research focuses on immunotherapy, or using the immune system to kill cancer cells. This research is an important potential addition to the current breast cancer treatment modalities of surgery, radiation and chemotherapy. Dr. McKee’s approach involves the creation of T cells, a type of white blood cell, for patient treatment through gene therapy. This treatment approach will allow us to bypass many intermediate steps which are necessary for natural T cell stimulation, and which have been obstacles to other immunotherapy methods. In addition, it will provide new opportunities to examine how cancer-fighting T cells travel through the body and interact with tumors.
As an Assistant Professor in the Department of Pathology at the University of Chicago, Dr. Frank’s laboratory investigates both the immune system and the mechanism of cancer development including leukemia and lymphoma. Dr. Frank’s research currently involves the study of two important processes. The first, the study of maintaining a normal immune system, called V(D)J recombination, and involves the generation of antibodies that all individuals require to fight infections. The second process involves the study of DNA repair. DNA in any cell can be damaged from exposure to radiation, environmental chemicals or from by-products of metabolism. When errors occur in these DNA breaks, the abnormal genes that are formed can lead to the development of cancer in any organ. Dr. Frank and her team wish to further their understanding of defects that can contribute to the development of cancer. Understanding these fundamental cellular mechanisms is a first step in the process of fighting cancer and designing specific therapeutic strategies.

As the Director of the Geriatric Oncology Fellowship Training Program and an Assistant Professor of Clinical Medicine at the University of Chicago, Dr. Rodin is currently studying the effects of cancer treatment on the cognitive performance of cancer survivors. She and her team are also implementing a research database project in the Cancer Survivor Clinic to examine the health care needs and health outcomes of elderly cancer survivors.
THE ASSOCIATE BOARD

Amanda Pierce, President

This is an organization of young Philanthropists committed to raising social awareness of cancer and to providing funds for immunology and for other programs in cancer research.

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FINANCIALS

**Beginning Balance July 1, 2002** $394,593

### Income

#### UCCRF Contributions
- Unrestricted: $354,020
- Restricted Fund: $372,842
  - **Total**: $726,862

#### Auxiliaries' Income
- Women's Board: $749,543
- Auxiliary Board: $64,998
- Associate Board: $22,685
  - **Total**: $837,226

#### Endowment Income
- UCCRF Board of Trustees: $4,213
- Simon M. Shubitz: $15,654
  - **Total**: $19,867

**Total Income** $1,583,955

### Expenses

#### Operating
- UCCRF: $171,738
- Women's Board: $246,419
- Associate Board: $12,259
  - **Total**: $430,416

#### Allocations
- Research & Faculty Support: $476,148
- Auxiliary Board: $90,000
- Women's Board: $547,000
  - **Total**: $1,113,148

**Total Expenses** $1,543,564

**Ending Balance June 30, 2003** $434,984
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