Intramural Faculties and Working Groups

Diverse Teams...

Building Solutions

Center for Cancer Research

Division of Cancer Epidemiology and Genetics

National Cancer Institute

Faculties & Working Groups

The Intramural Research Program (IRP) of the National Cancer Institute (NCI) is composed of the Division of Cancer Epidemiology and Genetics (DCEG) and the Center for Cancer Research (CCR). The focus and research philosophy of DCEG is to carry out an international program of population-based studies to identify environmental and genetic determinants of cancer. The mission of the CCR is to reduce the burden of cancer through exploration, scientific discovery, and translation of basic research to cancer prevention, diagnosis, and treatment. Together DCEG and CCR are able to pioneer novel approaches to translational and clinical research through their interdisciplinary research strengths.

To further capitalize on the diverse strengths of the IRP, Faculties and Working Groups were created to provide a forum in which scientists from diverse laboratories and branches can work cooperatively in a particular discipline, disease, or approach to scientific discovery. The Faculties and Working Groups cut across the traditional boundaries of Laboratory, Branch, and Division, and come together to foster collaboration, encourage open access to new technologies and clinical resources, facilitate drug, vaccine, and device development, and challenge NCI researchers to become more involved in multidisciplinary and interdisciplinary research.

NCI Intramural Principal Investigators may join any of the Faculties and Working Groups in which they wish to participate. Many groups also encourage Fellows, Staff Scientists, Clinicians, senior scientists and extramural science administrators from other Institutes and Centers to participate. In addition, some Faculties and Working Groups welcome members of the scientific community from outside of the NIH. Specific information, including membership requirements, is available on the individual Faculty and Working Group web sites.

For more information, visit the index of Faculties and Working Groups at http://ccr.cancer.gov/research/faculties_index.asp

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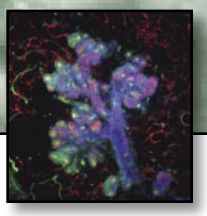


Breast Cancer

Chair
Barbara Vonderhaar

The Breast Cancer Faculty facilitates interactions among basic, epidemiological, translational, and clinical researchers promoting a community of investigators working together for the prevention, diagnosis, and cure of breast cancer. It welcomes the participation of scientists at all levels of their careers, both within and outside the NIH, as well as from the advocacy community.

Challenges to Progress

The lack of knowledge in the area of normal human mammary development was identified as a major impediment to the development of novel approaches to breast cancer prevention and treatment at the 2000 Retreat. A subcommittee was formed to spearhead a project to analyze frozen normal human breast tissues using several approaches, including cDNA microarray, proteomics, and tissue array. Preliminary laboratory work on the first phase of this project has begun. Normal human breast tissue samples are being collected and RNA is being extracted for microarray analysis. The Faculty has identified many challenges associated with this project, including tissue acquisition and sample quality, and is reaching out to the Maryland Organ Transplant Program and local medical hospitals to develop collaborations to facilitate this project.

Tissue Repositories

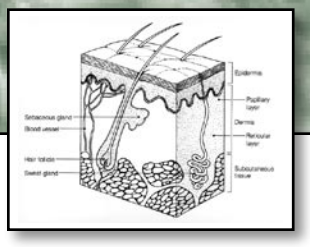
The Breast Cancer Faculty is developing a repository for breast tissue and tumor samples from clinical trials. The samples are appropriately processed, inventoried, linked to clinical data and (once released by pathology) anonymized for research purposes. These samples will be available to members of the Faculty for research purposes.

In parallel, normal mouse mammary glands from all stages of development have been collected, are maintained by the Faculty and are available to investigators by application. Frozen tissue from individual BALB/c and FVB mice is available for RNA, DNA and protein extraction, OCT frozen samples and formalin fixed tissue for sections. Tissue arrays of normal mouse mammary tissue at all stages of development have been prepared. In addition, a CD-ROM of mammary whole mounts (from FVB mice) at 17 stages of development is available to all interested members of the Breast Cancer Faculty.

Faculty Activities and Events

The Breast Cancer Faculty is extremely active. People interested in participating in the Faculty can attend a wide variety of events designed to advance the understanding of the molecular etiology, epidemiology, cell biology, prevention, and treatment of breast malignancies as well as to explore new opportunities and avenues of research, including developing and applying new technologies. A retreat is held each year to encourage interactions across scientific disciplines within the NIH and the research community outside, including colleagues in private practice, academia, and industry, as well as the breast cancer patient community, their families, and their caregivers. Roundtable Discussions are held regularly with in-depth discussions on cutting-edge topics and areas of research to foster and enable translational research. In addition, a monthly seminar series helps promote the career development of young breast cancer researchers by giving them opportunities to formally present their work with support of senior PIs and active mentoring. The Breast Cancer Faculty also regularly schedules a journal club, State of the Science meetings, and workshops. The schedule of Faculty-sponsored events is available through the web site below.

For more information about Faculty-sponsored events or to join this Faculty, please visit:
http://ccr.cancer.gov/research/faculties_index.asp



Cutaneous Carcinogenesis

Chairs

Stuart Yuspa / Margaret Tucker / Glenn Merlino

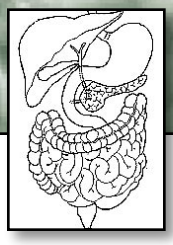
Recognizing the broad expertise and interest in cutaneous carcinogenesis that exists throughout the NCI intramural program, the Cutaneous Carcinogenesis Working Group consolidates and exploits those interests to advance our understanding of pathogenesis and develop novel approaches for the prevention, diagnosis and treatment of skin cancers.

Composed of epidemiologists, geneticists, basic cancer biologists, molecular biologists and clinicians, the working group brings together a cadre of experts to discuss novel ideas and collaborate on projects that constitute more comprehensive research programs on melanoma and non-melanoma skin cancers than would be possible with individual investigators.

The working group sponsors brainstorming sessions, retreats and outside speakers to accomplish its goal of open discussion to identify unsolved problems and develop collaborative solutions.

The Cutaneous Carcinogenesis Working Group invites NCI Principal Investigators, Fellows, Staff Scientists, Senior Clinicians, and senior scientists from other Institutes and Centers to participate. Membership is also open to local NCI Extramural Science Administrators.

For more information about this Group, visit:
http://ccr.cancer.gov/research/faculties_index.asp



Gastrointestinal Malignancies

Chair
Richard Alexander

The newly-formed GI Malignancies Faculty was created to coordinate the unique resources and expertise existing within the CCR and to make progress towards the common goals of improved prevention, early detection, and treatment of patients with cancers arising from the gastro-intestinal and hepato-pancreatic-biliary systems. Faculty members represent the disciplines of basic, clinical, and population sciences and membership is open to all colleagues within the NIH community. Participation in Faculty activities by others dedicated to our mission is strongly encouraged.

The Challenges of GI Malignancies

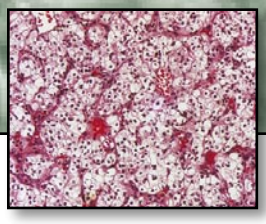
GI malignancies are the largest group of malignancies in the world, accounting annually for more than two million deaths, and over one-third of all cancer deaths, worldwide. In the United States there will be more than 250,000 patients diagnosed with cancer of the digestive system in 2003, and nearly 25% of all cancer deaths will be due to these malignancies. Particularly devastating is the fact that GI malignancies worldwide have very high disease-related mortality, exceeding 50% for colo-rectum, over 75% for esophagus and stomach, and approaching 100% for liver and pancreas. The GI Malignancies Faculty is dedicated to working closely with the discipline- and approach-based faculties to coordinate and apply the unique resources of the CCR to make significant advances for patients afflicted with these cancers.

Activities and Events

The GI Malignancies Faculty will meet on a monthly basis to hear presentations from members within the Faculty, promote exchange of ideas and information, and provide new opportunities for collaborations within the CCR community. Subsequent activities will be designed to expand dialogue between the GI Malignancies Faculty, other discipline-based and approach-based faculties and members of the extramural cancer community involved in digestive system cancers. The Faculty is working to serve as the natural venue for coordinating a robust translational and clinical gastrointestinal malignancy research program.

Faculty membership is open to all interested individuals including, but not limited to, NCI Principal Investigators, Staff Scientists, Clinicians, Postdoctoral Fellows, and technicians, as well as scientists from other Institutes and Centers. Membership is also open to local NCI Extramural Scientists.

For more information about Faculty activities or to join this Faculty, please visit: **http://ccr.cancer.gov/research/faculties_index.asp**



Genitourinary Malignancies

Chair
W. Marston Linehan

The goal of the Genitourinary Malignancies Faculty is to develop better methods for prevention, diagnosis and treatment of genitourinary malignancies. The current genitourinary malignancies of interest to this Faculty include cancer of the kidney, bladder, prostate and testis. The Genitourinary Malignancies Faculty has 85 members representing individuals from eighteen NIH Branches and Laboratories.

Communication Promotes Interdisciplinary Research

The Genitourinary Malignancies Faculty promotes an extraordinary amount of communication between the National Cancer Institute (NCI) branches and laboratories working on genitourinary malignancies, resulting in a high degree of interdisciplinary research. The Faculty plays an important role in recruiting outstanding urologic and medical oncology fellows, provides input to the NCI leadership on important issues regarding genitourinary malignancies, and was instrumental in the recently completed Kidney and Bladder Cancer Progress Review Group.

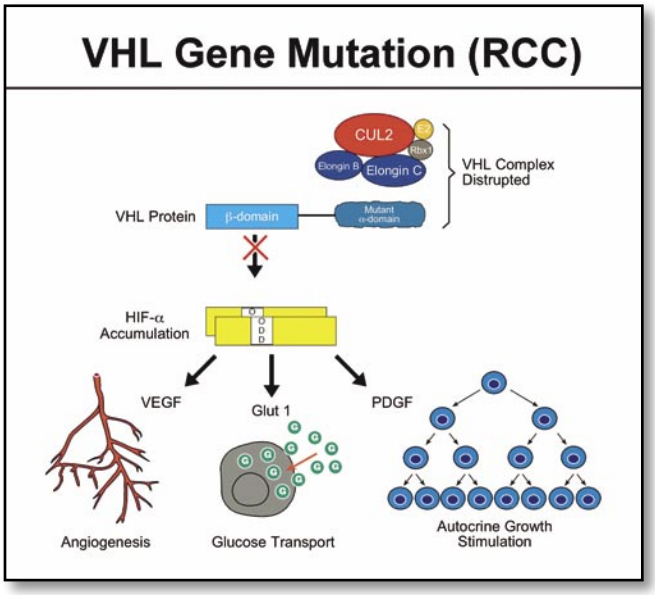
Closing Knowledge Gaps

The Genitourinary Malignancies Faculty is spearheading several initiatives to help close the knowledge gaps in kidney, bladder, prostate and testis cancer research. These projects include:

- studying the biochemistry of the Birt Hogg Dubé (BHD) gene
- collaborating with industry to study the genetic basis of familial renal carcinoma
- studying the genetic basis and genotype/phenotype associations with Hereditary Leiomyomatosis Renal Carcinoma
- analyzing kidney cancer patients for associations with HLA and natural killer cell receptor genes
- molecular imaging study of localized prostate cancer and seed implantation therapy trial of localized prostate cancer
- evaluation of c-Met pathway and HIF inhibitors in renal carcinoma
- clinical trial involving IL-2 and FGF vaccine in renal cell carcinoma
- using an animal model to test the ability of NK clones to kill RCC cells preferentially through KIR incompatibility
- optimizing the electro-fusion of human dendritic cells to RCC cells for the generation of tumor/dendritic hybrids for vaccine therapy.

Events and Accomplishments

The Genitourinary Malignancies Faculty promotes communication among its members and with the NIH research community by sponsoring a monthly seminar series, organizing an annual retreat at which current topics of interest are discussed and future directions are planned, and supporting visiting speakers to discuss important topics in cancer research.



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Genitourinary Malignancies

Accomplishments of the Faculty include:

- characterization of the Birt Hogg Dubé hereditary cancer syndrome
- discovery of a new cancer gene, the gene for Birt Hogg Dubé (BHD) and localization of the BHD gene on the short arm of chromosome 17
- demonstration of validation of cDNA microarray results with tissue array and layered expression scanning
- advances in genetics, diagnosis and localization of pheochromocytoma
- evaluation of anti-VEGF antibody therapy for patients with advanced renal cell carcinoma
- evaluation of the effectiveness of different dosages of IL-2 in patients with advanced renal cell carcinoma

Faculty membership is open to all interested individuals, including, but not limited to, Principal Investigators, Staff Scientists and Clinicians, Postdoctoral Fellows, technicians, and nurses.

For more information about this Faculty, visit:
http://ccr.cancer.gov/research/faculties_index.asp

Gynecologic Malignancies

Chair
Elise Kohn

The Gynecologic Malignancies Faculty promotes interactions among basic, population, translational and clinical researchers with interests in gynecologic malignancies. These interactions advance our understanding of the molecular etiology, epidemiology, prevention, cell biology and treatment of gynecologic malignancies and explore new opportunities. The Faculty fosters and enables translational research and encourages interaction across administrative boundaries at the NCI. The Faculty recognizes the many benefits of interacting with the gynecologic research community and endorses collaboration with extramural NCI, NIH, and our local practicing colleagues, academia, and industry. Faculty members have participated in DOD panels, Progress Review Groups, cooperative group and educational activities.

Educational Programs and Outreach

The Gynecologic Malignancies Faculty is actively involved in supporting educational programs in the community and within the Center for Cancer Research (CCR). Members of the Faculty are actively involved in the Ovarian Cancer National Alliance Leadership Training Program that is held here on the NIH campus each year. In addition, many of our members provide counsel to the Alliance on clinical and translational matters. Faculty members have also participated in Congressional briefings related to ovarian and other gynecologic cancers, as well as outreach educational programs to the local medical and lay community. It is our hope to expand and organize these efforts.

The Faculty recently hosted an Inter-Faculty retreat on Hormones and Cancer at Rocky Gap State Park. This retreat brought together colleagues from DCEG, CCR, DCP, and DCTD, with those from FDA and invited speakers. Gynecologic malignancies, breast cancer, and prostate cancer were the predominant topics. This retreat will spin off into more focused follow-up programs in the future. Discussions are underway with several faculties for joint seminar and retreat programs.

Physical and Virtual Repositories

The Gynecologic Malignancies Faculty is participating in the planning of both physical and virtual tissue repositories. Progress has been made in the interaction with the existing intramural physical repository in Frederick and in the generation of database elements for both the physical and virtual repositories. A manager is in place and is being trained for supervision of key repository functions, including tissue acquisition and storage, cell and fluid separations, fixation, and more advanced histological techniques. The Faculty sponsored a workshop related to these important processes.

Clinical Research and Training

The Gynecologic Malignancies Faculty has a focused interest in promoting clinical, translational, population and laboratory research and training in the gynecologic malignancies. This is being accomplished through collaborative development of clinical trials, outreach to the patient community, and development of training opportunities with Faculty members for gynecologic oncology fellows and clinicians and scientists interested in gynecologic cancers. The Faculty was integral in the reorganization and launch of the new NCI/Gynecologic Cancer Foundation Fellowship for junior faculty. Solicitations for the Fellowship are underway. A more formal training program in translational science of gynecologic malignancies is under development.

A Memorandum of Understanding is nearing completion for clinical collaboration with the Gynecology Oncology division at the Walter Reed Army Medical Center. This agreement will provide surgical support for Faculty clinical trials and also strengthen the clinical and training relationship between our institutions.

For more information about this Faculty, visit:
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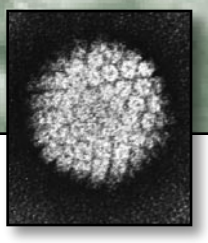

HPV

Chair
Douglas Lowy

The HPV Working Group (HPV-WG) serves as a forum to foster high-quality translational research with public health implications in the area of diseases induced by human papillomaviruses, with an emphasis on cervical cancer and its precursors. The HPV-WG seeks to use the available knowledge of the natural history of HPV infections and the pathogenesis of related cancers to foster both intra- and extramural research, with a goal of reducing the burden of HPV-related cancers. The members of the HPV-WG hope to frame specific concepts for consideration by NCI leadership. The ideas will accentuate interdivisional, inter-institute, and extramural sharing of resources and responsibilities to achieve our common goals.

Diversity Invigorates Information Exchange

The HPV-WG is composed of a broad and active group of intramural and extramural investigators from NCI and other parts of NIH. The diversity of the group is already fostering vigorous, practical debate regarding the best means to move from theory to reality, based on understanding of NIH scientific disciplines and funding mechanisms. Monthly meetings on a variety of topics, such as therapeutics and HPV vaccines, provide an opportunity for information sharing and enhance awareness of various relevant basic and translational research initiatives underway and currently under consideration. The exchange of knowledge, ideas, and research strategies among the diverse members of the HPV-WG provides information about the degree to which a proposed line of investigation is already part of another program, and the HPV-WG can make an informed judgment about whether to participate in this area and whether it might be beneficial to partner with another ongoing program. Alternately, this exchange of information may stimulate other areas of research which will be undertaken by other groups.

Focus on Prevention

The current major focus of the HPV-WG, with broad representation from CCR, DCEG, and several extramural NCI Divisions and Offices, is prevention-oriented research initiatives, which take maximum advantage of the expertise of the group. The goals of this research are to improve primary prevention (i.e., reducing the incidence or severity of incident HPV infection) and secondary prevention (i.e., reducing the likelihood that prevalent HPV infection will progress to invasive cancer). These goals will be achieved through careful consideration and promotion of research, development, and testing of more efficacious and/or more cost-effective diagnostic screening procedures, and interventions such as prophylactic and therapeutic vaccination. An important consideration will be examining how to increase the access of new technology for public sector providers, specifically those charged with extending the reach of cervical cancer prevention efforts.

For more information about this Faculty, visit:
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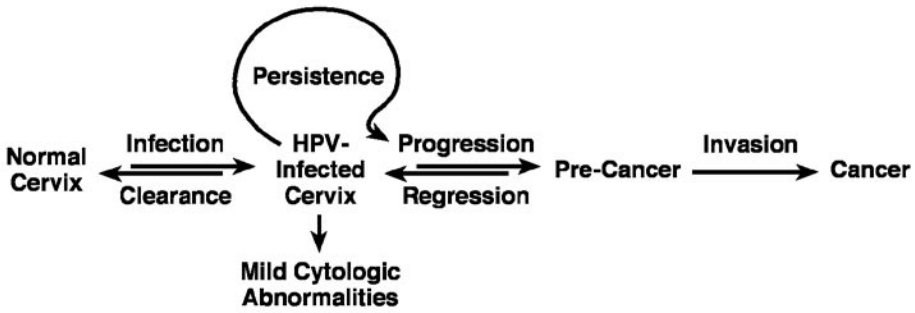
Natural History of Cervical Carcinogenesis



Lung Cancer and Upper Aerodigestive Chemoprevention

Chairs
James Mulshine / Len Neckers

The Lung Cancer and Upper Aerodigestive Chemoprevention Faculty applies molecularly targeted drug development to early aerodigestive cancers, investigates the dual needs of efficacy and safety of new drug delivery strategies, enhances intramural translational interactions, identifies and shares strategic resources that will enable relevant faculty research, serves as a mechanism for improving interactions with comparable research teams of extramural investigators and within the biotech and pharmaceutical industry, collaborates with Lung SPOREs (Specialized Programs of Research Excellence), focuses on problems of mutual interest, and combines participation in clinical trials. The Faculty serves to disseminate information on both basic and clinical advances in aerodigestive malignancies research to the NCI/NIH community and functions as an educational forum for investigators from diverse areas interested in aerodigestive malignancies. Membership is made up from NIH Principal Investigators, Staff Scientists and Clinicians, and Postdoctoral Fellows.

Faculty members collaborated with several SPORE sites to perform a randomized, placebo-controlled chemoprevention trial (Clinical Center 98-C-0118). In this trial, local delivery of a COX-containing oral rinse was well tolerated but produced no significant reduction in the extent of leukoplakia compared to the placebo. However, the favorable response rate to the placebo arm remains unexplained and further investigation of the tissue penetration with ketorolac is warranted. The results of this trial were presented at the 2003 American Society of Clinical Oncology Meeting in Chicago and discussed at the 11th SPORE Investigators' Workshop in Baltimore and will be published in Clinical Cancer Research.

The Aerodigestive Faculty submitted a research proposal for the Bioshield Initiative to develop clinical tools to manage individuals exposed to "dirty bombs." The proposal involves both diagnostic and therapeutic tool development based on the research work of NCI investigators, including our faculty members.

Projects Initiated

The Faculty has identified knowledge gaps in the area of lung cancer and upper aerodigestive research and has initiated the following projects to address them:

- Establish a mechanism for small-batch drug formulation to generate sufficient material for *in vivo* drug evaluation, using reagents with requisite stability and solubility
- Develop a mechanism for pilot evaluation of aerosolized drug delivery in rodent carcinogen-exposure models as a tool to evaluate relevant lead compounds
- Explore systems for optimizing epithelial drug delivery for intraepithelial neoplasia
- Initiate an early lung cancer screening trial with high resolution, spiral computerized tomography
- Create a venue to facilitate the evaluation of new targets for diagnostic or therapeutic intervention as well as to ensure candidates for participation in add-on investigator-initiated trials with new, molecularly targeted early therapies.
- Explore the utility of molecular targets, including retinoids, HDAC inhibitors, hsp90, PI3K, COX, and NF-kB, in the setting of early upper aerodigestive cancers.

Retreats and Workshops

Faculty retreats play a role in bringing together the members to discuss research opportunities that cut across NCI divisions and extend to the extramural community. The first Faculty retreat included a review of the members' Lung and Aerodigestive Research activities, presentations on collaborative opportunities from the Division of Cancer Treatment and Diagnosis (DCTD) and the Division of Cancer Prevention (DCP) scientists, and the establishment of a governance framework. The second retreat included reviews of new formulations for

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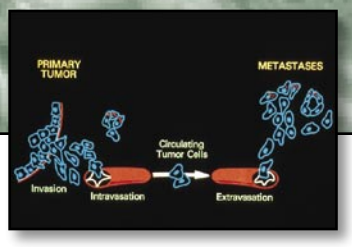
epithelial drug-delivery systems, strategies for analyzing complex data sets relative to clinical evaluation of drug effects, and CRADA (Cooperative Research and Development Agreement) strategies to enhance intramural translational research. To further the dialogue on drug delivery, the Aerodigestive Faculty held a workshop on September 15, 2003, entitled: Epithelial-Directed Drug Delivery: Influence of Formulation and Delivery Devices. A meeting report outlining the current state-of-the-art in pulmonary drug delivery from the presentations of several industry and academic leaders is being finalized.

For more information about this Faculty, visit:
http://ccr.cancer.gov/research/faculties_index.asp

Metastasis



Chair
Kent Hunter

The Metastasis Working Group (MWG) provides an environment for presentation and discussion of all aspects of research related to the dissemination and colonization of cancer to secondary sites. These interests include early detection of secondary cancer, basic research into the mechanisms of tumor spread, improved therapeutics, and chemoprevention strategies.

Collaboration and Information Sharing

The MWG serves as a forum through which members communicate, sharing and discussing current ideas, shifting paradigms, and emerging concepts in metastasis research. The goal of the MWG is to promote new collaborative interactions, develop and encourage novel approaches and strategies into the research and treatment of disseminated disease leveraging the combined experiences of the diverse member laboratories, and to augment communication between research groups, particularly between clinical and laboratory programs.

Interaction is crucial to fostering collaboration and information sharing and the MWG encourages interaction among its members and with other NCI faculties and working groups, including but not limited to, the Molecular Targets and Cancer Prevention Faculties, to further enhance a multi-disciplinary approach to studying metastatic disease. The MWG is planning retreats, thematic seminar series, and journal clubs to increase interaction among its members within the NIH, with adjunct members from outside NIH, and with other members of the scientific community.

The first Metastasis Working Group Retreat was held at the Marriot Hunt Valley on September 24-25, 2003. Invited speakers included Dr. Tom Parsons of the University of Virginia, Charlottesville, and Dr. Kenneth Yamada of NIDCR. The program included historical perspectives of metastasis research, current research and unanswered questions requiring future research. Two new projects are currently being pursued based on the discussions and interactions among the retreat participants.

Training, Education and Research Resources

A central priority of the MWG is the participation of postdoctoral fellows to further their training in the areas of metastasis research. Additionally, the MWG web site serves as an educational tool, with a central emphasis on disseminating publications of interest. A portion of the MWG web site has been named "Metastasite" and directs those interested to references to classical metastasis papers, frequently cited review articles, new directions in metastasis research, as well as metastasis experimental strategies available at NCI. It is a long-term goal of the MWG to develop "Metastasite" as a public-oriented educational resource.

Two major projects undertaken by the MWG are the generation of a metastasis gene "master list" as well as an all-inclusive metastasis pathway map. The creation of these items will provide a tool for researchers to more fully understand, recognize, and visualize critical points of interaction in the molecular mechanisms involved in metastasis. The MWG is also undertaking efforts to focus on the development of better *in vitro* and *in vivo* metastasis models, define prognostic markers relevant to metastasis in humans and to promote the use of RNAi in metastasis-related research.

The Metastasis Working Group invites NCI Principal Investigators, Fellows, Staff Scientists, Senior Clinicians, and senior scientists from other Institutes and Centers to participate. Membership is also open to local NCI Extramural Science Administrators.

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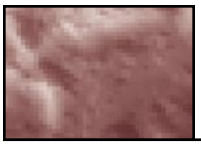


Discipline-based Faculties & Working Groups

Cancer Prevention Faculty

Cellular, Molecular, and Developmental Biology Faculty

Chemistry and Structural Biology Faculty

Clinical Immunotherapy Interest Group

Epidemiology and Carcinogenesis Faculty

HIV and Cancer Virology Faculty

Immunology Faculty

Stem Cell Working Group

Vascular Biology Faculty

Cancer Prevention

Chair
Nancy Colburn

The Cancer Prevention Faculty provides an intellectual focus for a cancer prevention program at the National Cancer Institute (NCI). This Faculty interacts with other Faculties and Programs, facilitates interdisciplinary collaborative research in prevention, and enhances access to technologies applicable to prevention research. The Faculty enhances communication among molecular biologists, mouse geneticists or developmental biologists, epidemiologists, and clinical oncologists, at all stages of their careers, from within and outside the NIH, who are interested in considering the molecular and cellular basis of multistage carcinogenesis to create molecular targeted and other strategies for cancer prevention.

Dr. Michael Sporn is working closely with the Faculty to help spearhead a major emphasis in Cancer Prevention in the Intramural Research Program. The formal inclusion of a prominent extramural investigator in this Faculty fosters the exchange of ideas, promotes new collaborations, and provides an atmosphere where novel approaches are proposed to prevent cancer.

Objectives and Initiatives

The Faculty has an ambitious series of objectives it is working hard to accomplish. It combines scientific strategies (e.g., combining cancer vaccines and chemoprevention) with proof-of-principle studies and cooperatively develops novel approaches and technologies. Several of its key objectives include demonstrating genes whose expression causes, prevents, or modifies susceptibility to carcinogenesis, at any stage of progression in any organ, using transgenic or targeted mouse models and showing that "hitting" the molecular target is effective for preventing progression without producing unacceptable side effects in the host.

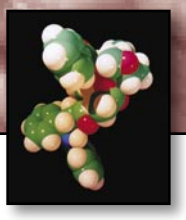
The Faculty has initiatives aimed at identifying small molecule drugs or dietary interventions, vaccines, or gene therapy reagents that modulate expression or activity of validated molecular targets, designing pre-clinical experiments to address pharmacokinetic and pharmacodynamic effects of potential preventive agents and to evaluate the effects of interventions on molecular targets, early biomarkers, and cancer endpoints. Finally, the Cancer Prevention Faculty has recognized a need for prevention studies in humans, especially as related to combinations of agents. The Faculty is planning human intervention studies to test the efficacy of single or combined interventions in modulating early biomarkers, cancer incidence, or progression.

Retreats Facilitate Communication

Faculty retreats have played a major role in bringing together members and non-members from within and outside the NIH to discuss research opportunities that cut across NCI divisions and extend to the extramural community. The Cancer Prevention Faculty retreats and the monthly seminar series, often co-hosted with other Faculties and Working Groups, provide forums for in-depth discussion about current topics in cancer prevention. The Fall 2003 Retreat brought together an array of experts to discuss and debate "The Ideal Mouse Model."

The Faculty evaluates existing strategies for pre-clinical and clinical prevention and makes recommendations to the NCI for new discovery experiments using mouse models, new molecular targets for cancer prevention, and new or better interventions. The Faculty assesses existing mouse models (e.g., for breast, lung, and colon cancer) for their capacity to address research questions in pre-clinical prevention studies and provides this information to other groups at the NCI, such as the Molecular Targets Faculty and the Vaccine Working Group. Cancer Prevention Faculty members are pursuing Collaborative Project Award (CPA) projects on melanoma prevention, lung carcinogenesis models, and selenium intervention. Finally, the faculty contributed to a grant proposal that is part of the NCI Mouse Models of Human Cancer Consortium (MMHCC).

For more information about this Faculty, visit:
http://ccr.cancer.gov/research/faculties_index.asp



Cellular, Molecular, and Developmental Biology

Chair
Gordon Hager

The Cellular, Molecular, and Developmental Biology (CMDB) Faculty provides a forum for presenting and discussing research related to the fundamental study of cellular and molecular biology. It is a community for investigators who wish to pursue common goals and projects in the basic sciences. This Faculty is active in bringing together members, sharing research findings, and building collaborations through the sponsorship of projects, workshops, special seminars, web site development, thematic retreats and special seminars.

Projects

The CMDB Faculty will sponsor projects from faculty members, including: multi-investigator collaborations, unique research proposals, training workshops for postdoctoral fellows and investigators, and workshops with outside experts focusing on technique and methodology. Currently, the Faculty is sponsoring a project to develop genome-wide promoter arrays for mice and humans that would permit a comprehensive analysis of transcription factors bound to all gene promoters under a variety of conditions using chromatin immunoprecipitation (ChIP). Sequence primers for these arrays will also be utilized to search for disease-related SNP's in the regulatory regions of human promoters.

Thematic Retreats

In 2003 the CMDB Faculty sponsored four retreats. The first retreat, "Receptors, Co-regulators and Hormone Action," entailed a wide breadth of seminar topics from various intramural researchers, including: "Nuclear Receptors and Chromatin," "THR Receptor Mutations in Disease," "Regulation of EGF Receptor Expression in Cancer Cells," "Multiple Prolactin Receptor Isoforms in Mammary Gland Development and Tumorigenesis," "ODD Transcription Factor Response to Hypoxia," and "Novel Transcriptional Approaches to Studying Molecular Signaling in Activated T Cells."

A second CMDB Faculty Retreat was held with the thematic focus of "Metastasis." The presentation topics included: "Genetic background is a major determinant of mammary tumor metastatic efficiency," "Genetic Determinants of Metastasis in Osteosarcoma," "Transgenic Mouse Models to Study the Roles of Tumor Cell and Environment in Metastasis," "Link between Ezrin-Associated Metastases and the Akt/mTOR/S6K1/4E BP1 Signaling Pathway Potential Therapeutic Implications," and "Positive and Negative Regulators of Metastases."

A third retreat was held on the theme of "New Techniques in Fluorescent Microscopy." The retreat seminars were as follows: "Overview of Techniques and Applications from a CCR Confocal Core," "A Collection of LSM 510 META-Inspired Projects," "Fluorescence Imaging Facility FRAP, FRET and FCS," "Imaging Movement: From Cells to Signaling Complexes," and "Confocal Microscopy in Frederick: Live Cell Imaging and Quantitative Image Analysis."

The final retreat featured the topic "Molecular Carcinogenesis" and included the presentations: "Induction and translocation of CLIC4, a p53 regulated chloride channel protein, participated in cell control, apoptosis and carcinogenesis," "The inhibitory effect of phytochemicals on aryl hydrocarbon induced carcinogenesis, " "Possible role of the antimutagenic pyrophosphohydrolase MTH1 in metal-induced carcinogenesis," "Predisposition to lung tumorigenesis by the lack of CC10, a major protein in the airway," and "Reactive oxygen as part of the contribution of mutant K-ras to malignancy in lung."

For more information about this Faculty, visit:
http://ccr.cancer.gov/faculties_index.asp

Chemistry and Structural Biology

Chair
Chris Michejda

Chemistry and Structural Biology (CSB) Faculty members perform basic research ranging from developing new concepts in rational and structure-based drug design to structural investigations at the atomic, molecular and cellular levels of resolution. Faculty membership is open to all interested PIs and Staff Scientists.

The Faculty continues to sponsor research seminars and has co-sponsored a one-day symposium on Surface Plasmon Resonance Spectroscopy, featuring several faculty speakers.

Training the Next Generation

Training the next generation of scientists with expertise in chemistry and structural biology is a high priority. To this end the Faculty is sponsoring a Program in Interdisciplinary Training in Chemistry, that is about to receive its first trainee. Successful trainee candidates will have two mentors: a chemist and a biologist. The program will be highly selective, serving to attract top chemistry Ph.D. graduates to the NCI, and the Chemistry and Structural Biology Faculty will participate in the selection process.

The Faculty participates in the Graduate Partnership Program in Chemistry. Participation in this program exploits NCI's unique environment at the interface of chemistry and biology. In addition, several members of the CSB Faculty have initiated interactions with New York University's Program in Structural Biology within the scope of the Graduate Partnership Program.

Participation with Molecular Targets Faculty

The Chemistry and Structural Biology Faculty facilitates interactions with other Faculties and Working Groups scientists and actively encourages collaborations in which their expertise can make significant contributions.

Several members of the Faculty have participated in the development of the Molecular Targets Development Program through the Molecular Targets Faculty. It is anticipated that the involvement of CSB Faculty in the Molecular Target Development Program will grow with time, since both chemistry and structural biology can make important contributions to the successful development of the concept.

Long-Term Visits

In an effort to reach out to the extramural community, the Faculty will sponsor long-term visits (6-12 months) to the NCI for up to two eminent chemists and structural biologists. These sabbatical-type visits will enhance the intellectual climate in these disciplines and will provide additional training experience to the postdoctoral fellows and graduate students. Professor Mariusz Jaskolski, an eminent structural biologist from Poland, will be the inaugural visitor in September 2004.

Activities Facilitate Communication

The Faculty sponsors seminar series, symposia, and an annual retreat in order to facilitate communication among its members as well as with people outside the Faculty both within and outside the NIH. The next Faculty retreat and workshop is planned for April 2004.

For more information about this Faculty, visit:
http://ccr.cancer.gov/research/faculties_index.asp

Clinical Immunotherapy

Chairs

I. Pastan / S. Rosenberg / T. Waldmann / K. Zoon

The Clinical Immunotherapy Interest Group serves as a resource for those scientists conducting translational research, specifically, those scientists who have an interest in tumor immunotherapeutic product development in the intramural community. The Interest Group hopes to create a research environment that is supportive of the pursuit of the most creative, cutting-edge basic and clinical research in immunotherapy development.

Building Collaborations and Resolving Barriers

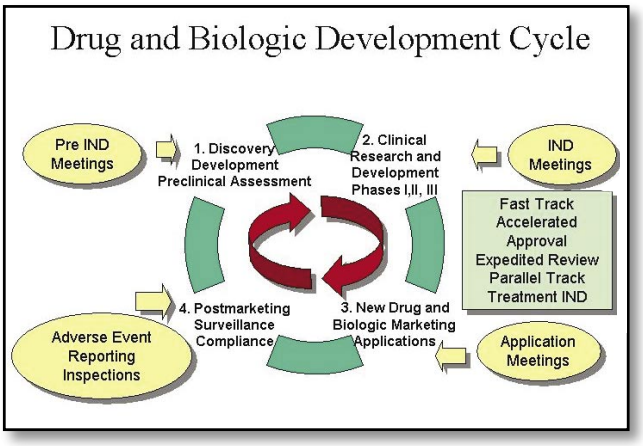
The Clinical Immunotherapy Interest Group is actively conducting discussions on barriers to clinical testing and product development and making recommendations for their resolution, sponsoring lectures to enhance the knowledge base of intramural investigators in translational medicine and regulatory and intellectual property issues, identifying opportunities to work with existing programs in the intramural and extramural programs, and building collaborations and utilizing contractors to assist in product development and regulatory issues. Through these efforts, the Group contributes to the goal of reducing the burden of cancer.

The Interest Group promotes communication among its members and with the NIH research community by sponsoring seminars and discussion sessions at which current topics of interest are discussed and future directions are planned. The seminar series fosters communication among Group members and provides continued information exchange as well as critical review of individual research efforts.

In 2003, the Group sponsored several seminars. Dr. Kathryn Zoon presented a discussion of the regulation and approval of drug and biological drug products. Dr. Ed Sausville presented a seminar on the NCI's Drug Therapeutics Program in areas including toxicology testing and product manufacturing and testing (BDP, Biopharmaceutical Development Program).

NCI Intramural Principal Investigators may join any of the Faculties in which they wish to participate. Although the Faculty membership is intended primarily for NCI Intramural PIs, Staff Scientists, Senior Clinicians, and senior scientists from other Institutes and Centers may participate. Membership is also open to local NCI Extramural Science Administrators.

For more information about this Working Group, visit:
http://ccr.cancer.gov/research/faculties_index.asp



Epidemiology and Carcinogenesis

Chair
Richard Hayes

The Epidemiology and Carcinogenesis Faculty seeks to promote and facilitate basic, clinical, and epidemiologic research by fostering increased communication among NCI scientists working in different disciplines on related target areas of carcinogenesis and epidemiologic research. The Faculty promotes and facilitates basic, clinical, and epidemiologic research, applying expertise in molecular biology, carcinogenesis, epidemiology and biostatistics to laboratory and population studies. As a forum for the exchange of ideas, the Faculty can foster research that may not have been possible through individual labs or branches. The Faculty plays an active role in organizing scientific meetings, seminars, workshops, and informal brainstorming sessions to stimulate research ideas. The Faculty also organizes working groups to encourage interdisciplinary scientific collaboration and cross-disciplinary meetings with other Faculties and provides opportunities for pre- and postdoctoral fellows to gain broader exposure to Faculty labs and branches.

The Epidemiology and Carcinogenesis Faculty is active in addressing emerging issues in the storage and processing of biospecimens. The NCI intramural program, comprised of CCR and DCEG, supports biorepositories that currently store over 7,000,000 specimens from over 500 studies. The NCI biospecimen support contractors also process thousands of specimens each year using standard protocols developed in collaboration with NCI investigators. Many of these specimens are blood components and urine samples collected for molecular epidemiology studies or clinical trials, requiring laboratory assays for micronutrients, pesticides, viruses, polycyclic hydrocarbons, water contaminants, endogenous hormones, and growth factors.

New Technologies and Analytical Strategies

With the establishment of high-throughput genotyping capacity at the NCI Core Genotyping Facility, studies are underway to identify genetic causes of common cancers. Also, multiple DCEG and CCR projects, some already in progress and others in the planning stages, will take advantage of new analytical strategies and technologies, including nanotechnology, proteomics, tissue micro-dissection, DNA and tissue arrays, and expression arrays. In addition to continuing to improve capabilities for collecting and cryopreserving blood, and extracting nucleic acids, there is also a need for increased proficiency in collecting and processing fresh, frozen, and paraffin-embedded tissues for advanced applications.

The Epidemiology and Carcinogenesis Faculty hosted a workshop focusing on the collection and processing of specimens, with special emphasis on new technologies. The goals of the workshop were to address practical questions concerning the relevant topics and to foster the development of standardized protocols. The workshop was organized into two major sessions: Blood Processing and Applications; and Tissue Processing and Microarrays, and was attended by 98 scientists from various NCI intramural and extramural programs, local NCI laboratory and biorepository contract personnel, other NCI support services contract personnel, and representatives of commercial organizations that are involved in developing specimen processing technologies. At the conclusion of the workshop, a series of recommendations were made for follow-up discussions, new methods development, and development of quality assurance protocols.

In addition to these efforts, the Epidemiology and Carcinogenesis Faculty has formed an intramural working group to identify the available resources for human molecular pathology at the NCI and to identify any specific resource gaps. Human molecular pathology is important for understanding the etiology of cancer, defining intermediate endpoints, clarifying the natural history of precursors, and identifying new screening and chemopreventive approaches. The Human Molecular Pathology Working Group is focused on defining the needs for molecular pathology, identifying unmet needs, and proposing

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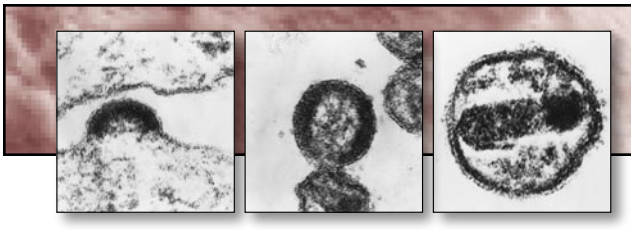
unified solutions to meet the identified gaps in molecular pathology support for the various types of ongoing intramural research. The CCR Laboratory of Pathology and the Human Molecular Pathology Working Group have identified a need for core infrastructure to meet the growing needs for quality assurance, batch testing, and rapid turnaround. The working group is also evaluating approaches to support large population-based studies.

For more information about this Faculty, visit:
http://ccr.cancer.gov/research/faculties_index.asp



HIV and Cancer Virology

Chair
George Pavlakis

The HIV and Cancer Virology Faculty promotes and facilitates basic, clinical, and epidemiological, interdisciplinary research on HIV, cancer-related viruses and other viruses. The scope of the research ranges from the understanding of the natural history and mechanisms of viral infection, pathogenesis and the host immune response, to the discovery of methods to prevent and treat viral disease, including the development of vaccines and treatments for HIV and cancer-related viruses.

Objectives

The HIV and Cancer Virology Faculty strives to increase communication and cross-fertilization of ideas among NCI scientists working in related disciplines. This is accomplished through facilitating the recruitment of new faculty, and recruiting and training postdoctoral and predoctoral fellows. The Faculty is working to identify and fulfill infrastructural needs to support these goals.

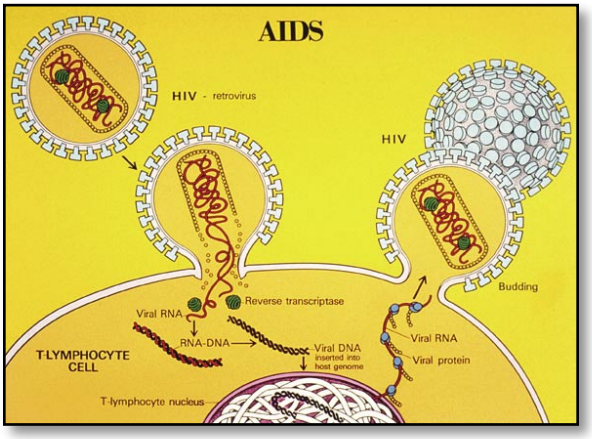
Retreats and Symposia

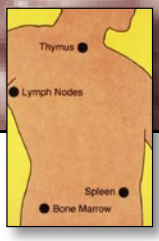
The HIV and Cancer Virology Faculty focuses on contributing to interdisciplinary scientific efforts by engaging in activities that facilitate the exchange of information and further collaborations. The Faculty holds regular scientific sessions where both NCI and extramural scientists present and discuss basic, clinical and epidemiologic topics in the areas of HIV and cancer virology. The Faculty has sponsored two one-day retreats in areas of the Faculty's interest. The theme of the first retreat was Future Vaccines for Papilloma and AIDS Viruses. The theme of the second retreat was Immunotherapy. This retreat brought together experts to discuss recent developments in immunotherapies for cancer and AIDS and the use of cytokines.

Members of the HIV and Cancer Virology Faculty have a dedication to contributing to both intramural activities and outside partnerships to further cross-cutting, interdisciplinary research. One example of the Faculty's continuous participation and commitment is the Third HIV Drug Resistance Program Symposium on Antiviral Drug Resistance. This event was organized by the HIV Drug Resistance Program of the NCI and the University of Pittsburgh. The Symposium brought together researchers in a variety of virus systems who share common interests in understanding the mechanism of action of the viral targets for resistance, the mechanism of antiviral therapy, and the mechanism of resistance to specific therapy.

The HIV and Cancer Virology Faculty invites NCI Principal Investigators, Fellows, Staff Scientists, Senior Clinicians, and senior scientists from other Institutes and Centers to participate. Membership is also open to local NCI Extramural Science Administrators.

For more information about this Faculty, visit:
http://ccr.cancer.gov/research/faculties_index.asp





Immunology

Chair
Steven Rosenberg

The Immunology Faculty is a collection of preeminent immunologists interested in understanding the immune system and engaging it to combat cancer in patients. To facilitate this, the Faculty disseminates information and encourages collaborations among investigators. The members also serve as valued advisors to the NCI Intramural leadership, identifying infrastructural and core needs to improve the quality of immunology research. Membership is open to all NCI Principal Investigators.

Seminars Stimulate Discussion

A major focus of the Faculty is a weekly seminar series, which brings the members together with other local and outside world-class immunologists to stimulate thought, discussion, and collaboration.

The seminar series has hosted discussions on subjects including the development of novel immunotherapies for solid tumors, understanding how tumors are protected from immune attack, *in vivo* requirements for the destruction of large established tumors by T cells, enhancing vaccines for HIV and cancer, regulation of T cell receptor turnover and T cell activation, development of vaccines for the human papillomavirus, use of a combination of vaccine and radiation therapy for established tumors, and immunology of host responses to renal cancer.

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For more information about this Faculty, visit:
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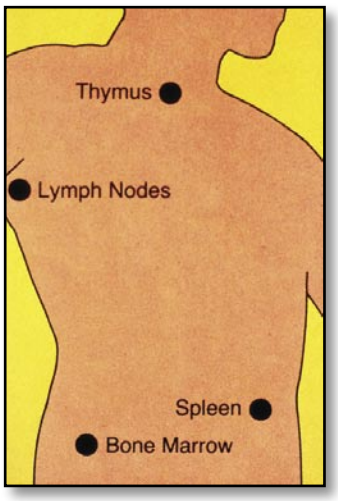
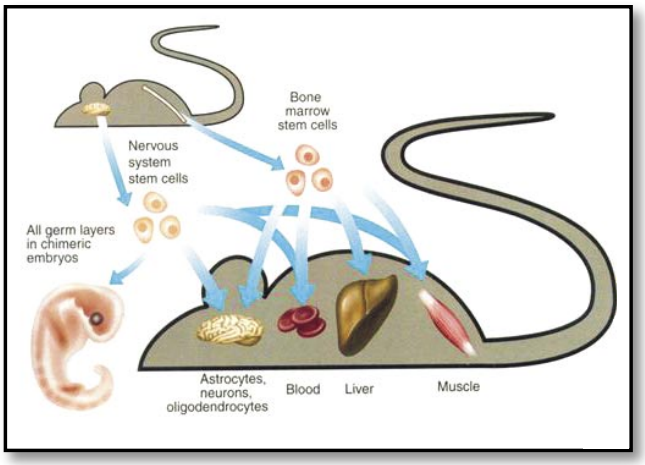


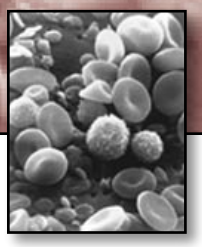
Stem Cell

Chair
Snorri Thorgeirsson

The Stem Cell Working Group disseminates information, encourages collaborations among investigators, and identifies needs to improve stem cell research in the NCI Intramural Program and throughout NIH. Topics of interest include fundamental stem cell biology, ontogeny, role of stem cells in oncology and the therapeutic potential of stem cells with particular emphasis on cancer. The Group is planning a seminar series and a retreat.

The Stem Cell Working Group invites NCI Principal Investigators, Fellows, Staff Scientists, Senior Clinicians, and senior scientists from other Institutes and Centers to participate. Membership is also open to local NCI Extramural Science Administrators.





Vascular Biology

Chair
William Stetler-Stevenson

The Vascular Biology Faculty seeks to create an intramural research community committed to the advancement and application of knowledge in the field of vasculogenesis and angiogenesis as applied to cancer treatment.

Promoting Excellence

The Faculty accomplishes this goal by promoting research excellence in the field of vascular biology in both the intramural and extramural communities and by creating a research environment that pursues the most creative, cutting-edge basic and clinical research in vascular biology, both as individual Principal Investigator (PI)-based initiatives as well as through collaborative interactions. Through these efforts, the Vascular Biology Faculty contributes to the goal of reducing the burden of cancer.

The Vascular Biology Faculty brings together National Cancer Institute (NCI) Intramural Investigators who have interests in topics related to vascular biology. The Faculty has created a program of research excellence and a national effort in discovery and translation of research achievements into novel cancer therapies.

Workshop Brings Together Experts

The Vascular Biology Faculty co-sponsored and participated in the Angiogenesis Monitoring in Clinical Trials Workshop at the Society for Biology Therapy Workshop. This workshop brought together internationally recognized experts in angiogenesis to discuss and propose community standards for the *in vivo* monitoring and testing of anti-angiogenic therapies currently under development. In addition to co-sponsoring this meeting, Faculty members participated in the formulation of recommendations for monitoring anti-angiogenic therapy in cancer patients, which will be published in the Journal of Immunotherapy.

Communication Stimulates Collaboration

The Vascular Biology Faculty promotes communication among its members and with the NIH research community by sponsoring seminars, organizing retreats at which current topics of interest are discussed and future directions are planned, supporting visiting speakers to discuss important topics in cancer research, and formulating long-range plans and objectives. The seminar series fosters communication among Faculty members and provides continued information exchange, as well as critical review of individual research efforts. This seminar series has also resulted in the formation of new collaborative efforts between Faculty members.

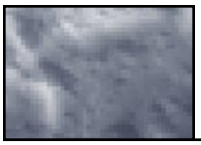
Networking encourages scientific excellence from all investigators and has led to ongoing collaborative efforts among laboratories. Two of these collaborations have led to applications for CCR Cooperative Project Awards (CPAs) and/or Intramural Research Awards (IRAs):

- A role for viral Interleukin-6 in the pathogenesis of Castleman's disease
- Effects of adrenomedulin gene-related peptides on normal/impaired wound healing

Angiogenesis Course for NIH

Recently, members of the Vascular Biology Faculty organized and presented a one-day course for NIH Intramural investigators on Angiogenesis Assays. The course material included information on several *in vitro* and *in vivo* angiogenesis assays, including the recently reported DIVAA (directed *in vivo* angiogenesis assay) system.

For more information about this Faculty, visit:
http://ccr.cancer.gov/research/faculties_index.asp



Approach-based Faculties, Working Groups & Initiatives

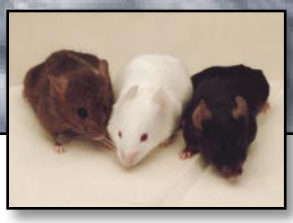
Animal Models

Bioinformatics, Biostatistics, and Computational Biology Faculty

Genetics, Genomics, and Proteomics Faculty

Molecular Targets Faculty

Vaccine Working Group



Animal Models

Chair
Glenn Merlino

The Animal Models Initiative (AMI) acts in an advisory capacity to the Director of the Center for Cancer Research (CCR), providing in-depth analyses of emerging trends in biomedical research. It is composed of NCI scientists proficient in clinical and veterinary medicine, biomedical technologies, molecular and classical genetics, bioinformatics and basic biomedical research. The AMI provides the intramural community with a synergy of expertise supporting the investigational use of animal models of human disease to illuminate the basic biology of cancer and to serve as a critical translational link between laboratory and clinic. It serves as a forum for collaboration within the intramural community, provides numerous training opportunities and facilitates interactions with extramural investigators.

Ongoing Projects

Animal Models Database

The AMI established the Intramural Animal Models Database to facilitate collaborations among NCI investigators and to ensure efficient access to animal models. This database is a resource of rodent strains housed at NCI. Some were developed in-house, others collected from collaborators and commercial suppliers. All principal investigators contribute information describing their rodent strains to the database. The Animal Models Database can be found at the following web site: http://ccr.cancer.gov/tech_initiatives/animalmodels/db/

Imaging

The AMI identifies and supports development of new and emerging technologies to image animals.

1. The AMI facilitated the establishment and maintenance of a mobile GFP/luciferase composite-imaging system for pilot use by CCR investigators. As the technology matures, AMI will ensure that CCR investigators continue to have access to the latest technology.
2. The AMI co-ordinates imaging technology development within the Comparative Molecular Pathology Unit (CMPU) that serves as a logistical and scientific resource for CCR scientists using the NIH Mouse Imaging Facility (MIF). The web site for the CMPU is http://ccr.cancer.gov/initiatives/Molecular_Pathology.asp
3. The AMI fostered development of a customized holding facility where rodents are permitted to leave and re-enter to enable NCI researchers to perform longitudinal studies in the MIF.

Developing Animal Models

Preclinical Animal Models

Animal models of human cancer are an important component in research, illuminating the basic biology of cancer and providing a critical translational link between laboratory and clinic. A Preclinical Animal Models Subcommittee was established to consider the conceptual and practical issues of using transgenic mice as tools for promoting translational research. As a result of Subcommittee deliberations, the Preclinical Models Strategy Team was established.

Technology Development

The AMI is facilitating (1) the creation of widely applicable inducible/conditional genetically engineered mice in consultation with CCR faculties, (2) access of CCR investigators to broad-spectrum transgenic mouse phenotyping, (3) development of mouse proteomics though a joint pilot project of the AMI, CMPU NCI-FDA Clinical Proteomics Unit and the Laboratory of Biosystems and Cancer.

Training and Education

Support

The Office of Mice Advice serves as a clearinghouse for assistance and contacts in all issues related to animal use for NCI.

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Animal Models

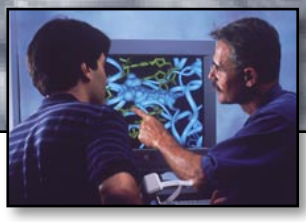
Training

Introduction to Using the Mouse as a Research Model at NCI (Mouse 102) is a symposium designed by the Office of Mice Advice to introduce NCI fellows, technicians and investigators to mouse-based research at NCI. Mouse 102 was filmed and is available as a long-term resource. Advanced topics in animal research will be presented in annual symposia.

AMI Seminar Discussion Series

To keep pace with rapidly advancing technology using animal models, the AMI sponsors the AMI Seminar Discussion Series in which prominent extramural researchers present seminars on their area of technical expertise and afterwards consider its development within the CCR. To facilitate interaction, relevant faculties are invited to cosponsor these discussions.

For more information about the AMI, please visit:
http://ccr.cancer.gov/tech_initiatives/animalmodels/default.asp



Bioinformatics, Biostatistics, and Computational Biology

Chair
John Weinstein

The Bioinformatics, Biostatistics, and Computational Biology Faculty works to promote research in bioinformatics, biostatistics, and computational biology and to encourage interactions among investigators at the NCI who have common interests in these disciplines – as well as those in other fields who use mathematical and computational tools. Given the growing importance of the information sciences in all areas of biomedical research – basic, translational, and clinical – the Faculty fosters studies and training across the entire spectrum of IT-based approaches.

With the ultimate goals of better diagnosis, prognosis, prevention, treatment, and management of human cancers, the Faculty encourages and facilitates communication between basic, translational, and clinical scientists in all areas of the NCI community, both intramural and extramural. To meet these goals the Faculty aims to facilitate development of core computational infrastructure and expertise to serve the needs of NCI researchers, and to facilitate recruitment and mentoring of fellows and other personnel. It also advises NCI leadership on infrastructure and programmatic initiatives.

Following extensive discussion, the Faculty Steering Committee developed a "Concept Proposal" for invigorating and augmenting informatics in the intramural program. Twin goals of the proposal are the promotion of intellectual excellence and the provision of core computational infrastructure and expertise to serve the needs of NCI researchers.

Collaborations and Activities

Successful Faculty collaborations include:

- designing an oligonucleotide-based promoter array to assess the genomic binding sites of transcription factors
- studying small non-coding RNAs in prokaryotes and, in combination with "wet lab" experiments, helping to identify the presence of two transcripts that negatively regulate expression of iron-storage proteins
- developing a pilot promoter array jointly with the Cellular, Molecular and Developmental Biology Faculty (in a collaboration between the NIA and NCI). This development can be expected to impact research across the NIH.
- with staff at the CIT, developing a widely used application for statistical analysis of microarray data
- in a collaboration between CCR laboratories, developing MatchMiner and GoMiner software for biological interpretation of microarray data

To further the goal of communication across the divisional lines of Branches and Laboratories, the Bioinformatics, Biostatistics, and Computational Biology Faculty supports retreats, a seminar series, a web site, and other informational resources. The Faculty has also surveyed NCI intramural researchers regarding infrastructural needs, and has made recommendations to the CCR leadership about the future of bioinformatics in the intramural program.

Membership is open to all NCI Principal Investigators, Fellows, Staff Scientists, Senior Clinicians and senior scientists from other Institutes and Centers, as well as extramural scientists.

For more information about this Faculty, visit:
http://ccr.cancer.gov/research/faculties_index.asp

Genetics, Genomics, and Proteomics

Chairs
Stephen Chanock / Jeffrey Strathern

The Genetics, Genomics, and Proteomics Faculty is interested in advancing research and promoting interactions among members of the National Cancer Institute (NCI) with common interests in classical genetics and high-throughput genomics and proteomics. It promotes long-term planning and implementation of new technologies and scientific approaches by encouraging collaborative research that crosses the administrative boundaries of laboratories and branches and enhances communication between basic, clinical, and epidemiological researchers.

Providing a Forum

The Faculty provides a forum for communication among researchers using classical genetics to address problems in basic and cancer biology. It also promotes interactions among Faculty members by supporting scientific retreats, a joint seminar series, and training programs. The Genetics, Genomics and Proteomics Faculty is composed of NCI Principal Investigators who are committed to the above-stated mission. The Faculty is led by a Steering Committee that communicates regularly.

The Faculty Supports:

- Collaborative Research Projects through interactions among faculty members
- A yearly Scientific Retreat to provide forums to establish and promote interactions
- A monthly seminar series to include a broad range of topics. Coordination with the OD/Office of Strategic Technologies is emphasized to present extramural and commercial scientists with a long-term vision of trends within a discipline
- Training programs to take advantage of the breadth and intellectual overlap of the Faculty
- Advocating for the development and improvement of the core facilities
- The translation of basic research to the clinical venue.

Close ties with other faculties are fostered. For example, close cooperation and joint projects with the Bioinformatics, Biostatistics and Computational Biology Faculty are being developed to support complex data retrieval, analysis and display problems. Joint meetings/lectures could be part of the regularly scheduled meetings. Additionally, a partnership with the Epidemiology and Carcinogenesis Faculty is being pursued.

Workshops Highlight Evolving Approaches

The GG&P Faculty sponsored a highly informative meeting on molecular approaches to detect changes in gene copy number. Deletions and amplifications are common mechanisms of altering gene expression levels in tumor cells. Characterization of such genome rearrangements provides clues to the identification of genes that suppress or promote tumor formation. Several techniques, collectively called Comparative Gene Hybridization, have been developed to detect deletions and gene amplification.

The workshop highlighted three array-based approaches. The human or mouse genomes can be arrayed as about 30,000 overlapping clones of over 150 kb in Bacterial Artificial Chromosomes (BAC). A comparison of hybridization of normal and tumor derived DNAs to these BAC arrays can detect deletions as short as 50 kb and even smaller gene amplifications if present in high copy number. Some investigators reported successfully using the cDNA-based microarrays, originally developed to monitor RNA expression levels, to screen for changes in gene copy number. While this approach is also capable of detecting deletions and amplifications with a resolution similar to the BAC arrays, it is currently limited by the extent of coverage of the genome represented by the cDNAs. The use of oligonucleotide-based microarrays is

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still in the development stage. The signal-to-noise ratio is too low at present to allow the whole genome to be used as a probe. However, methods were described that showed differences between normal and tumor genomes can be detected by choosing comparable subfractions of the DNA.

It is clear that these powerful approaches are still evolving and the Genetics, Genomics, and Proteomics Faculty will continue to follow their development and to promote the application of these techniques in our research. The Faculty is planning another meeting on the use of microarrays to monitor gene expression and the interpretation of those data.

For more information about this Faculty, visit:
http://ccr.cancer.gov/research/faculties_index.asp

Molecular Targets

Chairs
Pat Steeg / Carl Barrett

The Molecular Targets Faculty provides the infrastructure to facilitate collaborative basic, translational, and clinical research on molecular targets or pathways. The primary focus of the Faculty is the identification, validation and preclinical intervention into molecular pathways, with the goal of developing new cancer therapeutics within the Intramural Research Program (IRP). The Faculty aims to provide collaborative advice and infrastructure to this unique and worthwhile effort. The Molecular Targets Faculty welcomes the participation of scientists at all levels of their career both within and outside the NIH.

Molecular Programs

Discussions among Molecular Targets Faculty members identified prominent "holes" in the research capabilities of the IRP with respect to the drug development and validation process. To address these issues the Faculty has launched two programs, the Molecular Targets Development Program and the Molecular Therapeutics Program.

The Molecular Targets Development Program (MTDP) specializes in the development and application of high-throughput screening assays for molecular targets under investigation in the intramural program. Using a team approach, investigators experienced in high-throughput assays, organic chemistry, and the isolation of natural products develop and validate screening assays to identify small-molecule inhibitors and biologic agents that interact with molecular targets. The MTDP supports and facilitates some of the preclinical development of promising molecular targeted compounds, as well as the development of new research reagents. An equally important focus of the MTDP is the training of predoctoral and postdoctoral scientists in the interdisciplinary fields necessary for bioassay development and molecularly targeted drug discovery.

The Molecular Therapeutics Program (MTP) is another program being implemented by the Molecular Targets Faculty and will provide additional infrastructure for preclinical drug development. Molecular oncology will assist investigators in mechanistic investigations, as well as the identification of drug combinations likely to be effective in clinical trials. Preclinical pharmacokinetics will be available to intramural investigators performing mouse or other preclinical tests. Advice on several aspects of chemistry, including structural optimization and formulation, will be provided on a committee basis. The MTP also participates in the Preclinical Models Strategy Team, which is attempting to develop relevant preclinical models for drug development.

Pipeline Symposium

The Faculty recognizes that the identification and validation of new molecular targets, the preclinical development of drugs and the conduct of groundbreaking clinical trials require a group of multi-disciplinary investigators. The Faculty inaugurated a "Pipeline" Symposium in 2003, to be conducted semi-annually. At the first Pipeline Symposium, intramural researchers met with representatives of the NCI Developmental Therapeutics Program and Cancer Therapy Evaluation Program, as well as the FDA, to discuss progress on eight compounds, ranging in development from validation of the target to projected Phase I trials. Translational teams have been formed around four of these compounds and the teams have defined goals and assigned research responsibilities. Examples of the team approach include the successful application for a new clinical trial, microarray analysis of preclinical model data, examination of a compound as a radiosensitizer, and participation in a group meeting concerning the formulation of a compound.

Communication and Education

Retreats, seminars and other educational activities bring together not only the members of the Molecular Targets Faculty, but members from other Faculties and Working Groups, NCI and NIH investigators, and participants from the extramural community to

(continued on reverse)

discuss research opportunities that cut across NCI divisions and extend to the extramural community. The Faculty sponsors an annual retreat where multiple projects are presented and strategic goals are discussed. They also participate in the Molecular Partnership Seminar Series, which brings together intramural investigators and biotechnology companies. The Faculty co-sponsored an educational tool, the Drug Development Primer to teach the basics of drug development and clinical testing. Members of the Molecular Targets Faculty participate in the CCR Preclinical Models Strategy Team to collaboratively develop good models for leading compounds, assess preclinical pharmacokinetic and pharmaco-dynamic research needs and make recommendations to the IRP leadership. These programs and events are key to this Faculty's success in stimulating innovative concepts and practices to further the development of new, molecularly targeted cancer therapeutics in the IRP.

For more information about this Faculty, visit:
http://ccr.cancer.gov/research/faculties_index.asp

Vaccine Working Group

Chairs
Jay Berzofsky / Larry Kwak

Members of this group are carrying out an ambitious program to harness the power of the immune system to treat and prevent cancer, as well as HIV and viruses that cause cancer. Recent advances in basic immunological research have increased our understanding of immune mechanisms to allow the translation of these basic discoveries to the immunotherapy of cancer. New approaches have been developed to identify tumor antigens to incorporate into vaccines. Further, newly discovered immunological principles have led to second-generation vaccine approaches that allow for the induction of an immune response that is not only stronger, but also more appropriate for elimination of tumor cells.

Consensus and Collaboration

The Group has worked to develop a consensus on issues such as identification of tumor antigens, and determination of relevant and effective assays for evaluating immunologic responses to cancer vaccines, and approaches to immunization, and monitoring of disease. The Group has also been actively collaborating with the Cancer Genome Anatomy Project (CGAP) to develop strategies to mine the CGAP database to identify potential new tumor antigens. Through collaboration with the Clinical Proteomics group, a proteomic approach is used to identify new tumor antigens.

Identifying Needs

In addition, the Group has identified current infrastructural needs for vaccine trials and has made recommendations for Phase II clinical trial designs for vaccine trials and coordinated novel Phase III cancer vaccine trials by the intramural program. The Group formed a committee to study trial design for cancer vaccines, which require a different approach from the conventional chemotherapy-based model. This committee published a major article on cancer vaccine trial design in the Journal of Clinical Oncology as a useful guide for investigators undertaking cancer vaccine trials, as well as for IRBs and regulatory agencies evaluating clinical protocols for vaccines.

Reorganization of Support Services

The Vaccine Working Group took responsibility for the reorganization and oversight of the central NCI contract with SAIC for monitoring immunologic responses. The Group reviewed and assessed existing approaches to centralized monitoring of immunologic responses at institutions with successful programs, and formed an oversight committee for the contract. The committee recommended major reorganization, and is supervising the development and validation of assays, providing ongoing oversight of the SAIC Lab, and reviewing proposals for new work to be done at SAIC. As a result, the Clinical Support Lab has been reorganized, and has developed and validated assays, such as ELISPOT and cytokine induction, under supervision of the committee. These assays can be requested by NCI investigators when needed for monitoring immune responses in their clinical trials.

Sponsored Symposia

The Vaccine Working Group has jointly sponsored different symposia to further collaboration and information sharing on topics pertinent to different faculties. Together with the HIV and Cancer Virology Faculty a symposium was held on Vaccines for HIV and for Human Papillomavirus. A symposium with the Breast Cancer Faculty and the MOCRU Breast Cancer Unit focused on Vaccine Immunotherapy of Breast Cancer, and a symposium with the Cancer Prevention Models Faculty addressed Animal Models of Cancer.

The Vaccine Working Group invites NCI Principal Investigators, Fellows, Staff Scientists, Senior Clinicians, local NCI Extramural Science Administrators, and senior scientists from other Institutes and Centers to participate.

For more information about this Group, visit:
http://ccr.cancer.gov/research/faculties_index.asp

Newly Formed Faculties and Working Groups

Discipline-Based

Integrative Biology Faculty

Approach-Based

Nanotechnology Working Group