THE CANCER LETTER

P.O. Box 15189 Washington, D.C. 20003 Telephone 202-543-7665

Vol. 15 No. 48
Dec. 15, 1989

Price $185 Per Year North America
$200 Per Year Elsewhere

Reviewers Report Progress In New Drug Prescreen System Development, Commend DTP

NCI undertook a major change in its Developmental Therapeutics Program five years ago, deciding to drop the mouse tumor panels in use as a prescreen since 1975 in favor of new system utilizing in vitro

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In Brief

Durant Says He Expects Comprehensive Centers Lineup To Change With New System

"I EXPECT that some existing comprehensive cancer centers will lose that designation and some new ones will gain it. That is good. It will make the system more egalitarian": John Durant, who as chairman of the National Cancer Advisory Board's Centers Committee led the effort to revamp requirements for recognition by NCI of comprehensive center designation. Durant said he was satisfied with the new requirements and review guidelines, and, for now, with the move of the Cancer Centers Branch to the Div. of Cancer Biology & Diagnosis, "where it was welcomed with enthusiasm". . . . **CANCELED:** January meeting of the Div. of Cancer Prevention & Control Board of Scientific Counselors. Plans had called for the entire meeting to be devoted to a workshop on diet and breast cancer; the NCAB's decision not to fund the Diet FIT trial made it inappropriate to hold the workshop at this time. Next meeting of the DCPC board will be in mid-May. . . . **NCI STAFF** appointments: **Claude Klee**, who has been acting chief of the Laboratory of Biochemistry in DCBD, has received permanent appointment to the position; **Gordon Cragg**, acting chief of the Natural Products Branch in the Div. of Cancer Treatment's Developmental Therapeutics Program, is the permanent chief; **Margaret Holmes** has been named acting chief of the Cancer Centers Branch in DCBD's Centers, Training & Resources Program. . . . **"WE HAVE,** I hope, embarrassed HCFA and the Blues about their policies on reimbursement. The silly business about labeling drugs experimental without differentiating between those that are truly investigational and those that are prescribed for off label uses is ridiculous": Louis Lasagna, chairman of the National Committee to Review Procedures for Approval of New Drugs for Cancer & AIDS. Speaking at the recent NCAB meeting, Lasagna also criticized third party payers for not reimbursing treatment IND and Group C drugs. . . . **CORRECTION:** Arvin Glicksman, professor and chairman of the Brown Univ. Dept. of Radiation Medicine and chairman of radiation oncology at Roger Williams General Hospital, was incorrectly identified in the Dec. 1 issue of **The Cancer Letter.** He is not affiliated with Univ. of Pennsylvania.

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Reviewers Report Progress In New Drug Prescreen System Development

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screens with human tumor cell lines. The mouse tumor panels, dominated by the P388 leukemia prescreen, failed to find compounds with clinical activity against common solid tumors in man.

The new concept involved development of several panels of characterized and calibrated human tumor cell lines, representative of a range of tumor types, as a prescreen. Once tumor type selectivity has been identified, a compound progresses through human tumor xenograft assays in the nude mouse and thence through conventional toxicologic and pharmacologic assessments.

The concept was novel, and controversial in some quarters. Some doubted it would work; that apparently is not an issue now. There is evidence that the system can identify agents with tissue selective cytotoxicities. Development of the new system has been a major undertaking, however. Although all the required elements still are not yet in place, considerable progress has been made.

An ad hoc review committee has been keeping an eye on the project, conducting rigorous and detailed reviews annually. The committee met last month to develop an overview of the program, and wrote a report on its status, along with a number of recommendations. Chief among them was that "the screening project be fully implemented by DCT without delay and with the highest priority. Further, it anticipates that a period of three to five years may be required before its impact on new drug discovery can be reliably assessed."

The report praised DTP Director Michael Boyd for his "outstanding scientific and managerial qualities. Without his single minded determination, enthusiasm, and selfless leadership, it is quite clear that this project would never have reached its present status of achievement."

The report noted that the project "should be seen to have dimensions not only of national, but also of international significance," a point demonstrated in the makeup of the ad hoc committee, which is chaired by Kenneth Harrap of the Institute of Cancer Research in Surrey, England. "DCT has been a world leader in promoting discovery of novel anticancer drugs. While its resources are clearly not limitless, they surpass those available elsewhere. This program is not only essential, but it may also be of pivotal importance to drug discovery worldwide for at least the next decade. Seen in this context, the project is unquestionably a valid and legitimate pursuit for NCI."

Additional excerpts from the report follow:

Program objectives have been addressed by both extramural and intramural staff and by the PRI (Program Resources Inc., the primary contractor at Frederick Cancer Research Facility). The need for coordinated research and development has become critically apparent. To achieve this, Dr. Boyd has organized and manages directly a DTP intramural unit, the Program Development Research Group (PDRG), at FCRF. This group is responsible for the development and refinement of primary and secondary screening assays (both for the antitumor and anti-HIV screens), the development and characterization of cell lines used in the screens, and for the isolation and detailed chemical and biological characterization of new leads from natural product extracts found active in either of the two primary screens.

Resources

Staff members in the project are of high scientific quality. The numbers devoted to the screening operation are probably sufficient to achieve the program objectives. However, the chemistry initiative is seriously understaffed; the complement of chemists needs to be expanded commensurate with the program requirements.

For adequate performance of the R&D, there should be close geographic proximity of the key functional components. Unfortunately, current space constraints at FCRF present a severe compromise. The intramural chemistry staff are spread between two different buildings (in one case, using borrowed space in the contractor operated extraction lab, causing a major shortfall of that essential effort and an escalating backlog of unprocessed samples in the repository). The PDRG biology staff is similarly fragmented, with staff both on site and FCRF and in Bethesda.

Also, the committee finds it quite incredulous that

THE CANCER LETTER

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ISSN 096-3917. Published 48 times a year by The Cancer Letter Inc., also publisher of The Clinical Cancer Letter and AIDS Update.

major pieces of new equipment essential to the tasks of this group remain in storage due to lack of space for installation and operation. There should be a high priority for providing the needed space at FCRF to enable the unification of this group.

In view of the magnitude and complexity of the project, the scientific achievements have been remarkable in the relatively short time span of five years. Cell line panels representative of a range of tumor types have been assembled, characterized, and calibrated. A reliable assay method has been developed and appropriate data handling arrangements are now in place. Scale up of the screening operation to meet the desired compound throughput has been achieved. A 60 cell line panel is now in place and sound evidence has been presented that the screening model does indeed possess the ability to identify molecules exhibiting tissue selective cytotoxicities. There seems every likelihood that new candidates for clinical evaluation may well derive from this venture during the next five years or so, a potential time frame which must be considered as highly acceptable.

The staff is to be congratulated for the great strides made in overcoming the computer problems that seriously hampered the program in the past. However, additional opportunities exist to refine further the processes of data evaluation, and every effort should be made to make the database more easily and readily accessible to all the program scientists.

Quantitative Analysis of Screening Data

The "mean graph display" and the COMPARE program provide a good starting point for quantitative analysis of the screening data. Simply put, the goal of such analyses is to pick a winner (an agent with selective cytotoxicity) from among all the compounds screened. In the most optimistic scenario, agents with tissue selective cytotoxicities will clearly stand out in the mean graph displays, and only a cursory eyeball analysis will be needed.

However, in the event that such an optimistic scenario does not unfold, continuing effort should be expended on exploring alternative means of data analysis. Particular effort should be devoted to coupling biological intuition with quantitative analysis, in order to explore and study further all the various factors that interact to influence the screen and the screening results.

Regardless of the method of analysis chosen, the criteria used to select an agent as a potential winner should be clearly and analytically formulated.

Several statistical approaches adopted by separate staff members need coordination. In the absence of some mechanism for more closely linking these efforts, the committee urged a reconsideration of its previous recommendation that a professional biostatistician (preferably possessing cell biology expertise) be appointed or consulted.

Cell Line Panels

The absence of breast and prostate tumor lines was of some concern, although it was noted that efforts to raise examples of these were ongoing under contract. Only one squamous tumor (lung) was included. When these lines become available, it is suggested they be added to the model in blocks, or alternatively are used to replace the brain tumor lines. Where replacement of individual lines is thought to be appropriate, an important consideration should be the maintenance of diversity within the panels.

Much discussion revolved around the question of assay duration in the slowly growing lines, where one doubling might no occur during the period of exposure. Project staff is urged to devote some research effort to this problem, specifically to develop further slow growing tumor lines and to inquire of the possible dependence between exposure time and chemosensitivity in such lines. It was suggested that an assay duration of at least four days, preferably longer, would be appropriate.

Screening Results

A 48 hour drug exposure time and a protein assay endpoint (sulforhodamine B) have been adopted routinely. Data analysis is via the mean graph display and the COMPARE algorithm which enable pattern recognition and closest match comparisons. Such techniques detect readily the comparable tissue selectivities of structurally related compounds and those of chemicals which have common mechanisms of action. Throughput is likely to reach 400 compounds per week in the near future, providing a realistic objective of 20,000 compounds per year.

Some interesting data were reported on the unexpected sensitivity of the brain tumor panel to FUdR, while four ellipticine derivatives also exhibited unique selectivities in this panel. Some 2,150 natural product extracts have been screened in a pilot study and a few of those have shown particular sensitivity for melanoma cell lines.

The model is calibrated routinely against 175 standard agents (comprising NDA, IND and DN drugs), the reproducibility of repeat calibrations being remarkably good.

In light of these findings the committee recommended unanimously that the present 60 cell line primary screening model be fully implemented without delay (spring 1990?). It was clear that this panel had already demonstrated its ability to

recognize at least some new examples of cell line selective chemosensitivities. The potential benefits of expanding the panel to 120 lines (proposed by the investigators) should be weighed against the potential disadvantage of compromising high screen throughput. Moreover, expansion of the present cell line panels would delay further the full implementation of the screening program, now seen by the committee to be an issue of serious urgency. However, the option of replacing some of the lines with others more suitable (particularly squamous, mammary, and/or prostate) should be retained as they become available.

Strategy In Selecting, Identifying Actives

The major effort has been devoted to elaborating and refining a screening model with the capacity to identify tissue selective cytotoxicities. This has now been achieved. Further R&D will now be required on compounds which exhibit novel chemosensitivity. In particular, where several structurally disparate chemicals, or where several analogs of a particular molecule, display similar mean graph profiles, how will they be prioritized for further development? Possibilities include in vitro evaluation against a larger panel of calibrated cell lines of the same tissue type as those in which sensitivity was observed in the primary screen; evaluation in the nude mouse xenograft model; a combination of both; identification of the biochemical determinants which render cells susceptible to unique compounds and their analogs. This might be achieved through collaboration with other laboratories according to their particular interests.

Human Tumor Xenograft Assays

Fifty eight lines have been implanted subcutaneously in the nude mouse. Forty six grew, of which 35 were regarded as suitable for testing purposes. Calibration of the latter against 12 standard agents is almost complete. This has been an outstanding sabbatical achievement organized by Heiner Fiebig. Limited xenograft evaluation of two leads has been initiated, but these experiments are not yet sufficiently advanced.

The program proposals in relation to xenograft studies and the associated pharmacologic and toxicologic objectives have not been previously presented to the committee and there was little opportunity to discuss these topics during the review. The suggestion was made that the task order mechanisms might be a means whereby other laboratories might be recruited to this activity. An FCRF based pharmacology laboratory would probably be more appropriate, although it was observed that in house expertise may well be available, both in Bethesda and at Frederick. It is important that a strategy for determining this issue be developed in the near future. It was also suggested that the investigators convene a workshop to address these issues soon. Further, it will be important to recruit additional specialized staff, including those with both tumor biology and pharmacology expertise to develop further these aspects of the program.

Natural Products Initiative

The staff is to be congratulated on its accomplishments in establishing an efficient program for the collection and processing of natural products, and for the assay in the primary screen. Much intelligent thought has gone into devising the way in which natural materials are processed and assayed, and the derived data represent an important resource that can be used to facilitate the identification of novel lead structures with antitumor and anti-AIDS activity. The program has already demonstrated its capacity to discover several novel anti-HIV leads, with more potential products in the pipeline. The interfacing of the natural products resource with the antitumor screen is now actively under way and is progressing well. A pilot screening study has already shown evidence of its ability to identify extracts possessing interesting panel specific activity.

Because the goals of the program can be met only if the natural product leads are pursued vigorously and the active constituents isolated and characterized structurally, a substantial increase in the number of chemists involved in fractionation of extracts and structure elucidation is recommended as an urgent priority. The nature of the laboratory facilities that they require should be addressed in parallel.

"The concept is quite simple, but we've found over the last five years that converting the concept to reality is quite a challenge," Boyd said in discussing the program last week with the National Cancer Advisory Board.

"I would like to go on record," NCAB member Enrico Mihich said, "that within the number of cells used, and within its other limitations, the screen is going much better than before, and in fact quite well. I commend Mike Boyd for that.

"On the other hand, the initial concern I had was not so much whether a perfect screen could be established, but it was a conceptual one. The screen can determine activity against one cell. It can select a specific agent, but not selective agents. On another hand, the mouse screen we've been using for decades has enormous limitations. We must continue with this program. I agree with the recommendation on verifying with xenografts. Then and only then can we demonstrate the value of the project. But I don't think

the xenografts should be in stage 2. They should be stage 1, right up front."

"Henry made the point I wanted to make," NCAB member Gertrude Elion said. "There's nothing magic about 60 or 120 cell lines, if the compound is destroyed in vivo before it gets to the tumor."

Suitable Mechanism, Funding Source Were Issues In Diet FIT Controversy

More on the aftermath of the National Cancer Advisory Board's decision not to fund the Diet FIT trial:

There remains considerable doubt on the part of some regarding the scientific issues (fat vs. calories, validity of the epidemiology studies which provide the rationale), and some question the need for an expensive large scale clinical trial given the apparent trend toward less fat in the American diet. But the major reason for not funding the trial is the cost, $60 million over 10 years.

The cost factor in this case was compounded by the issue of whether the RO1 mechanism was appropriate for this study. This is a year in which less than 20 percent of new and competing RO1 grants will be funded by NIH. Removing $12 million from the RO1 pool would have chopped that percentage to an intolerable figure.

Even without the budget squeeze, is the RO1 mechanism appropriate for a large, multi-institutional study that extends over 10 years? NCAB members attempted to address that issue, without coming to any conclusion. At the open session following their unanimous vote reaffirming their earlier decision not to fund Diet FIT, they considered whether NCI and NIH should accept such large investigator initiated grant applications. Board member Howard Temin, contending that RO1 grants of that size "could destroy the system," offered a motion calling for a cap. Others felt a dollar limit might not be legal and that it might also inhibit individual creativity. Temin withdrew his motion when it was agreed the issue would be brought up at the next meeting.

Diet FIT's principal investigators, Maureen Henderson and Ross Prentice, did not have an RO1 in mind when they wrote the grant. They felt it would be feasible as a program project. But NCI's Div. of Extramural Activities determined that it did not fit the requirements of a PO1, so it was ruled an RO1.

Diet FIT was an attempt to continue the effort to study the impact of dietary fat reduction on cancer rates. Its predecessor, the Women's Health Trial, was going to look only at the impact on breast cancer incidence. Diet FIT added colon cancer and heart disease. The Women's Health Trial was to be funded entirely out of the Div. of Cancer Prevention & Control's appropriations earmarked for cancer control. That would not have had any impact therefore on the RO1 pool; it would have been funded through cooperative agreements with the participating institutions.

DCPC Director Peter Greenwald told **The Cancer Letter** last week that he would have considered providing some of the Diet FIT money out of his cancer control budget. The National Heart, Lung & Blood Institute also indicated it might share in the cost, if NCI had decided to go ahead with it.

The Women's Health Trial was killed by the DCPC Board of Scientific Counselors, in part at least because of the cost and subsequent impact on the tightly squeezed DCPC cancer control budget. But the same board (basically, with a few new members) favored going ahead with Diet FIT, in part because of the additional endpoints and streamlined design (WHT would have cost about $100 million), and presumably also because the money would not have come out of the DCPC budget.

"I don't look at this as being over," Greenwald said. "I still think that a study of the impact of fat reduction on cancer incidence is a creditable, major part of cancer prevention. I assume that we can eventually think this through and support some kind of diet trial."

In a presentation to the NCAB during an open session on dietary prevention of cancer, Greenwald cited new epidemiology studies which support the hypothesis: Italian women emigrating to Australia experienced an increase in breast cancer incidence faster than Japanese women immigrants in the U.S.; Lawrence Kolonel's study of five ethnic groups found a strong correlation of fat intake and breast cancer; A California study of Seventh Day Adventists found in a group which averages 32 percent of calories from dietary fat (40-45 percent U.S. average), the incidence of colorectal cancer is 70 percent that of the U.S. average, breast cancer 72 percent, and overall mortality is 30 percent less.

"I'm not contending the hypothesis is proven," Greenwald said. "Only that there is enough evidence to warrant a study to prove it one way or another. We have a strong hypothesis for a major public health problem. I don't see how we can clear up this question without some kind of clinical trial."

"I have reduced my dietary fat, and every magazine and newspaper I read says we should reduce fat," Temin argued. "So what would the public health

impact be, granted (fat reduction) is so heavily prescribed?"

"It's one thing to say, 'Do this while research continues,' and another to say 'Definitely do this,'" Greenwald responded. "We also need better evidence on time relationships. There is a big question for persons in their 50s and 60s, if it can have an impact on incidence."

Board member Erwin Bettinghaus suggested that a large randomized trial in which the control group is not provided information on the possible health impact of dietary fat might not be ethical.

Greenwald said that both controls and intervention participants would be told they should reduce fat intake. "The fact is, controls don't do it," while those in the intervention group go to meetings, are frequently contacted and encouraged to stay on the diet.

Board member Gertrude Elion suggested that epidemiology studies were sufficient to prove the hypothesis. "What if we had taken the attitude that epidemiology studies were not enough in smoking?"

"Epidemiology did give us that answer. It was clear cut," Greenwald said. "It is not so clear in dietary fat."

Final Issue Of The Decade; Office Closed, But Not Phone Or Fax

This issue of **The Cancer Letter**, Number 48 of Volume 15, is the final issue of the year, and the decade as well. The next issue, Volume 16, Number 1, will be dated Jan. 5, 1990.

The staff of **The Cancer Letter** will take some time off during the next two weeks, perhaps joining you in reflecting on the momentous events of the 1980s, in cancer research and other matters affecting the state of the world. We can all hope that during the 1990s we will realize some of the benefits of those events.

The Cancer Letter office will remain open through Dec. 22, and will be open again Jan. 2. Some staff members will be on hand during that time. When no one is around, the answering machine will be on, and the fax machine never sleeps.

Warmest best wishes for the holiday season and New Year.

Minority CCOP Applications Not Yet Reviewed; Will Go To NCAB In May

The 23 applications NCI received for its new Minority Community Clinical Oncology Program have not yet been reviewed, as stated in **The Cancer Letter** Dec. 1.

Those applications will be reviewed in late February or early March, with the results going to the National Cancer Advisory Board at its May meeting. NCI plans to make the awards effective June 1.

NCI/FDA Joint Training Program Approved By HHS; Begins In July

An NCI/FDA joint training program has been approved by HHS and will begin next summer to train at least two young scientists per year in what NCI Director Samuel Broder calls "regulatory medicine."

The three year fellowship program will provide formal training in clinical trials design and management. The NCI/FDA fellows will work in NCI's Cancer Therapy Evaluation Program and FDA's Center for Drug Evaluation Research.

The fellowship program was the idea of Div. of Cancer Treatment Director Bruce Chabner, as part of the recent effort to improve relations between NCI and FDA.

In February, NCI and FDA staff members began holding monthly meetings to try to reach agreement on drug development issues. "We have made significant progress, but we don't agree on everything," Chabner told the President's Cancer Panel this week. "Most of those remaining issues involve endpoints for drug approval.

"One problem both of us face is the lack of suitably trained young people in clinical trials design. FDA has found it difficult to find those interested in this career."

Now, however, with a major explosion of activity in drug development, "there is an accute need in industry and government for people interested in drug development," Chabner said.

The program will start with only two trainees per year for the three year program. However, Chabner said that if suitable applicants can be found, the program may be able to accommodate more trainees.

During the first year of the program, trainees will participate in clinical work at NCI. In the second and third years, the clinical work will be combined with work at FDA.

FDA Commissioner Frank Young told the panel that there are four applicants for the program, which will begin in July.

"I think this program may solve our differences," Chabner said. "If people with the same training and background are working at both FDA and NCI, we may have no differences over endpoints."

Chabner called it "a unique opportunity for a young person not necessarily interested in bench research to

get into clinical trials management. "My one fear is, we will train people who will be nipped off by industry," he said.

Young noted that FDA has no training program analogous to NCI's. "If we can retain 50 percent of the people involved in the program, it will be a great help."

Chabner said the effort to attract young scientists to NIH has been helped by a change in attitude about the Public Health Service, partly as a result of the visibility and leadership of former Surgeon General C. Everett Koop. "For years we had lost a cadre of people who went into Civil Service instead of PHS," Chabner said. There were no salary advantages in PHS and less of a career track, he said. Some of that is now changing.

Broder suggested that if the training program is successful in encouraging young scientists to take jobs at FDA, perhaps the medical school loans of the trainees could be forgiven, as is the case for certain young scientists who decide to go into AIDS research.

Young also told the President's Cancer Panel that because of the better relations between the two entities, FDA and NCI have been able to collaborate on treatment investigational new drug applications and have improved joint research efforts.

Young said he hoped NCI and FDA would be able to collaborate on the following problems:

--Definition of phase 2 and 3 clinical trials
--Definition of endpoints
--Guidelines for drug approval
--Development of quality of life endpoints

Any progress in these areas "will result in bringing new cancer therapies to patients more quickly," he said.

Chabner brought up the issue of reimbursement for Group C and treatment IND drugs, which NCI and FDA consider equal. He noted that at meetings of the National Committee to Review Current Procedures for Approval of New Drugs for Cancer & AIDS (the Lasagna Committee), insurance representatives have said they felt that standards for deciding which drugs would get the treatment IND status were "fuzzy."

"Insurers are balking at paying for these," Chabner said. "Should we continue to combine Group C and treatment IND?"

Young said he thought the categories should remain as they are, "because it is a way to signal earlier evaluation. It has helped move drugs through the process faster.

"The lack of reimbursement for treatment IND is unconscionable," Young continued. "These drugs are on their way through the system."

Young emphasized that the treatment IND and Group C drugs are much farther along in the process than those just entering phase 2.

About 80 to 95 percent of treatment IND and Group C drugs are later approved for marketing. In comparison, Young said, about 60 to 70 percent of drugs that enter phase 2 trials will not be approved.

Assistant Secretary for Health James Mason, in his first appearance before the President's Cancer Panel, commended the panel members--Armand Hammer, William Longmire and John Montgomery--for their years of service. Noting that if the years of each member's service were combined (24 years), it would equal a career in public service. "I want to express my appreciation for what you're doing," he said. Mason also commended Broder for his first year as NCI director. "I don't know an individual in PHS who keeps me informed better than Sam Broder," he said.

Mason said one of five priorities that were set by HHS Secretary Louis Sullivan for the department was to enhance the nation's biomedical research capacity. "You can't enhance America's biomedical capacity without enhancing NIH," Mason said. In that context, "We'll be looking at funding and trying to reverse the recent trends." Mason said that in defending the 1990 budget, Sullivan took a strong position in fighting budget cuts favored by the White House Office of Management & Budget.

Part of the effort to ehance NIH will involve improving the infrastructure, which has been neglected, Mason said. Salaries are another concern. The Congressional pay raise added "an initial chunk," but "we're not near the point where NIH can compete with industry and academia," he said.

NCI Advisory Group, Other Cancer Meetings For Jan., Feb. Future

Sixth National Cancer Communications Conference--Jan. 10-12, Washington. Sponsored by NCI and American Cancer Society. Contact Communications Conference, 1801 Rockville Pike, Suite 500, Rockville, MD 20852, phone 301/468-6338.

11th Congress, Assoc. of Radiation Oncologists of India--Jan. 11-14, Nagpur, India. Contact Dr. Harish Kulkarni, Cancer Centre, Manewada Rd, Nagpur 440 003, India.

Meeting Patient and Family Support and Referral Needs--Jan. 11, 18 and 25, Pennsylvania State Univ., McKeesport Campus, McKeesport, PA. Contact Denise Brooks, 412/624-7899.

Egyptian Society of Tumor Markers Oncology/Mediterranean Society of Tumor Markers

Oncology--Jan. 16-19, Cairo, Egypt. Contact Dr. Omar El-Ahmady, Oncology Diagnostics Unit, Biochemistry Dept., Faculty of Medicine, Ain Shams Univ., Abbassia, Cairo, Egypt, phone 2(02)2611650.

Ionizing Radiation Damage to DNA: Molecular Aspects--Jan. 16-21, Lake Tahoe, CA. Sponsored by Radiation Research Society. Contact UCLA Symposia, 2032 Armacost Ave, Los Angeles, CA 90025.

Cancer Biotherapy Symposium--Jan. 17-18, Orlando, FL. Sponsored by Orlando Regional Medical Center, Biological Therapy Institute, and National Biotherapy Study Group. NBSG semiannual meeting immediately follows symposium. Contact Patti Devlin, Orlando Regional Medical Center, 1414 Kuhl Ave., Orlando, FL 32806, phone 1-800-648-0450.

6th Annual Cancer Symposium--Jan. 18, Mosul, Iraq. Contact Dr. Ayad H. Al-Ramadhani, Iraqi Cancer Society, Mosul Branch, PO Box 760, Mosul, Iraq.

Molecular Basis of Cellular Adhesion--Jan. 20-26, Steamboat Springs, CO. Sponsored by Benentech and Glaxo. Contact UCLA Symposia, 2032 Armacost Ave., Los Angeles, CA 90025.

Teaching Course on Brachytherapy--Jan. 22-26, Villejuif, France. Contact ESTRO Secretariat, Dept. Radiotherapy, VH St. Rafael Capucijnenvoer 35, 3000 Leuven, Belgium.

American Cancer Society National Conference on Advances in Cancer Imaging--Jan. 24-26, New York. Contact ACS, 1599 Clifton Rd NE, Atlanta, GA 30329, phone 404/329-7604.

National Cancer Advisory Board--Jan 29-31, NIH Bldg 31C. Open 8:30 a.m.-5 pm on Jan. 29-30; 8 a.m.-1 p.m. on Jan. 31.

Postgraduate Institute for Pathologists in Clinical Cytopathology--Course A, Home Study, from February-April, and In-Residence Course B, April 23-May 4, an intensive program in all aspects of clinical cytopathology, for certified pathologists. Contact Dr. John Frost or Betty Ann Remley, 111 Pathology Bldg, Johns Hopkins Hospital, Baltimore, MD 21205, phone 301/955-8594.

Society of Gynecologic Oncologists Annual Meeting--Feb. 4-7, Fairmont Hotel, San Francisco. Contact SGO, 111 E. Wacker Drive, Suite 600, Chicago, IL 60601.

Indian Society of Oncology/Workshops on Pain and Lasers--Feb. 7-12, Ahmedabad, India. Contact Gujarat Cancer & Research Institute, Civil Hospital, Campus, Awarwa, Ahmedabad 380 016 India.

Cancer Management Course--Feb. 10-11, Honolulu, HI. Contact Dr. Scott Hundahl, American College of Surgeons, Cancer Dept., 55 E. Erie St., Chicago, IL 60611, phone 312/664-4050.

Steroid Receptors, Transcription Factors and Gene Expression--Feb. 10-13, Catamaran Resort Hotel, San Diego, CA. Contact American Assn. for Cancer Research, 330 Market St. 2nd Floor, Philadelphia, PA 19106, phone 215/440-9300.

New Trends in the Management of Cancer--Feb. 13-24, Cairo, Egypt. Contact Prof. Shawki El-Haddad, Kasr-El-Aini Center of Oncology and Nuclear Medicine, El-Manial, Cairo, Egypt.

Southwest Oncology Nursing Symposium: Challenges and Opportunities in Cancer Nursing II--Feb. 16-17, Phoenix, AZ. Contact Debbie Todd, Outreach Services, Good Samaritan Regional Medical Center, 1111 E. McDowell Rd, Phoenix, AZ 85006, phone 602/239-5994.

Meeting Patient and Family Support and Referral Needs--Feb. 16 and 23, Univ. of Pittsburgh School of Nursing, Victoria Bldg, Pittsburgh, PA. Contact Denise Brooks, 412/624-7899.

Novel Chemotherapeutic Approaches in Treatment of Colorectal Cancer--Feb. 23-24. Doral Ocean Beach Resort, Miami Beach, FL. Contact Div. of Continuing Medical Education (D23-3), Univ. of Miami School of Medicine, PO Box 016960, Miami, FL 33101, phone 305/547-6706.

24th Annual Clinical Symposium--Feb. 23, St. Jude Children's Research Hospital, Memphis, TN. Contact Director, St. Jude Children's Research Hospital, Box 318, Memphis, TN 38101, phone 901/522-0300.

UICC Cancer Nursing Workshop--Feb. 25-30, Mexico City, Mexico. Contact Dr. J. de la Garza, Instituto Nacional de Cancerologia, Av. San Fernando No. 2, Tlalpan, 14000 Mexico D.F., Mexico.

Supportive Care in Cancer Patients--Feb. 28-March 3, St. Gallen, Switzerland. Contact Congress Secretariat "SUP-90," Med. Klinik C, Kantonsspital, 9007 St. Gallen, Switzerland.

FUTURE MEETINGS

Diagnosis and Treatment of Neoplastic Disorders: Medical, Surgical and Radiotherapeutic Aspects--March 29-30, Johns Hopkins Medical Institutions, Baltimore, MD. Contact Office of Continuing Education, Turner Bldg, 720 Rutland Ave., Baltimore, MD 21205, phone 301/955-2959.

Molecular Targets for Cancer Chemotherapy: The Dorothy Snider Foundation Forum on Cancer Research--April 20, Memphis, TN. Contact Dr. James Hamner, Univ. of Tennessee-Memphis, 847 Monroe Suite 235, Memphis, TN 38163, 901/528-6354.

Topics in Clinical Medicine--May 14-18, Johns Hopkins Medical Institutions, Baltimore, MD. Contact Office of Continuing Education, Turner Bldg, 720 Rutland Ave., Baltimore, MD 21205, phone 301/955-2959.