The research programs will distribute $17.8 million in NIH Common Fund support in fiscal year 2010 and additional funds in future years. The projects capitalize on emerging scientific opportunities and technology advances to fuel biomedical discovery, strengthen the biomedical community nationally and globally, and hasten the translation of science discoveries into new and better treatments. Included in the 7 programs are initiatives with direct relevance to molecular imaging and therapy research. Among the new initiatives are: (1) the Library of Integrated Network-Based Cellular Signatures Program, which will build a community resource of scientific information to drive understanding of the ways in which components of biological systems, such as genes and proteins, function normally to maintain health or become disrupted by genetic and environmental stressors to cause disease; (2) the Protein Capture Reagents Program, which will create a suite of high-quality, affordable, and reliable new research tools to isolate proteins to study their function under normal conditions and when the cell is stressed or diseased; (3) the Knockout Mouse Phenotyping Program, which will be an international partnership to decipher the ways in which specific genes control certain characteristics or phenotypes in mice; (4) the Science of Behavior Change Program, which will examine ways in which human biology, culture, and society together influence ability to adopt and maintain healthy behaviors; (5) the NIH Induced Pluripotent Stem Cell Center, which will be a national center to drive the translation of scientific knowledge about stem cell biology into new cell-based treatments; (6) the Global Health Program, which will explore ways to increase capacity for global health research by enhancing education, training, and research opportunities in developing countries; and (7) the Regulatory Science Program, a collaboration between NIH and the Food and Drug Administration, which will encourage rapid and efficient use of new knowledge, technologies, and innovations in the development, investigation, and regulatory review of medical products.

Additional information about the NIH Common Fund can be found at http://commonfund.nih.gov.

National Institutes of Health

FROM THE LITERATURE

Each month the editor of Newsline selects articles on diagnostic, therapeutic, research, and practice issues from a range of international publications. Most selections come from outside the standard canon of nuclear medicine and radiology journals. These briefs are offered as a monthly window on the broad arena of medical and scientific endeavor in which nuclear medicine now plays an essential role. We have added a special section on molecular imaging, including both radionuclide-based and other molecular imaging efforts, in recognition of the extraordinary activity and promise of diagnostic and therapeutic progress in this area. The lines between diagnosis and therapy are sometimes blurred, as radiolabels are increasingly used as adjuncts to therapy and/or as active agents in therapeutic regimens, and these shifting lines are reflected in the briefs presented here. We have also added a small section on noteworthy reviews of the literature.

MOLECULAR IMAGING

Imaging VEGF Receptor Response

In the February issue of *Translational Oncology* (2010;3:56–64), Blankenberg et al. from Stanford University (CA) reported on the development of a molecular imaging tracer for imaging vascular endothelial growth factor receptor (VEGFR) response to antiangiogenic therapy. The tracer, ^{99m}Tc-scVEGF, is an engineered single-chain form of radiolabeled VEGF. When injected intravenously in mice, the tracer preferentially binds to and is internalized by VEGFRs expressed in tumor vasculature. The article details the ability of VEGFR imaging to monitor the effects of pazopanib, a small-molecule tyrosine kinase inhibitor under clinical development. Pazopanib selectively targets VEGFR, platelet-derived growth factor receptor, and c-Kit receptors in mice with HT29 human colon tumor xenografts. The ability of the VEGFR imaging to accurately assess pazopanib-induced decreases in numbers of VEGFR-2$^+$/CD31$^+$ endothelial cells in the tumor vasculature was confirmed at histologic analysis. The authors concluded by suggesting that "VEGFR imaging can be used for the identification of patients that are responding to VEGFR-targeted therapies and for guidance in rational design, dosing, and schedules for combination regimens of antiangiogenic treatment."

Translational Oncology

Intraoperative NIRF Cholangiography

In an article in the February issue of the *World Journal of Surgery* (2010; 34:336–343), Figueiredo et al. from the Massachusetts General Hospital and Harvard Medical School (Charlestown, MA) reported on a new near-infrared fluorescent (NIRF) agent that

is rapidly excreted via the biliary route in preclinical models to facilitate intraoperative real-time NIRF cholangiography. A lipophilic NIRF agent with hepatobiliary excretion was injected intravenously into 5 groups of mice, including experimentally induced chronic biliary obstruction, acute biliary obstruction, bile duct perforation, choledocholithiasis, and a group of controls. The biliary system was imaged for 1 h in all mice with NIR fluorescence and an intraoperative small animal imaging system. Extrahepatic ducts and extraluminal bile were clearly visible, with target-to-background ratios peaking at 25 min postinjection and signal visible for 1 h. Rapid identification of biliary obstruction, bile duct perforation, and choledocholithiasis was possible. The authors concluded that NIRF agents with hepatobiliary excretion "may be used intraoperatively to visualize extrahepatic biliary anatomy and physiology" and that "in conjunction with laparoscopic imaging technologies, the use of this technique should enhance hepatobiliary surgery."

World Journal of Surgery

SPIO-Affibody MR Imaging of HER-2

Konshita et al. from the Osaka University Graduate School of Medicine (Japan) reported in the February 8 issue of *Contrast Media and Molecular Imaging* (2010;5:18–22) on the combined use of an HER-2 targeting affibody, a small (7-kDa) molecule that behaves in ways similar to antibodies, and superparamagnetic iron oxide (SPIO) for noninvasive MR imaging of HER-2–expressing cells and tissues in vitro and in vivo. The authors described initial studies in a murine tumor xenograft and concluded that "affibody-SPIO is a feasible, target-specific contrast agent for in vivo MR molecular imaging."

Contrast Media and Molecular Imaging

Novel NIRF Imaging of $\alpha_v\beta_3$ Expression

In an article in the February issue of *Molecular Imaging* (2010;9:21–29), Liu et al. from the Stanford University School of Medicine (CA) reported on noninvasive visualization of tumor integrin $\alpha_v\beta_3$ expression using near-infrared fluorescence (NIRF) imaging of an infrared dye–labeled new cyclic RGD dimer with tetra(ethylene glycol) (PEG4) linkers in a U87MG (human glioblastoma–astrocytoma) tumor model. The authors described confirmation of $\alpha_v\beta_3$ binding in in vitro cell staining, as well as positive results in in vivo and ex vivo NIRF imaging. These findings were compared with histologic results, which demonstrated both tumor vasculature and tumor cell integrin $\alpha_v\beta_3$ binding in vivo. They concluded that NIRF imaging with this novel agent "offers an easy, fast, and low-cost way to detect and semiquantify tumor integrin $\alpha_v\beta_3$ expression in living subjects."

Molecular Imaging

THERAPY

Novel RIT Approach in Cervical Cancer

Phaeton et al. from the Albert Einstein College of Medicine/Cancer Center (Bronx, NY) reported in the February 15 issue of *Cancer* (2010; 116[S4]:1067–1074) on the influence of proteasome inhibitor MG132, external radiation, and unlabeled antibody on tumor uptake and biodistribution of ^{188}Re-labeled anti-E6 C1P5 antibody in cervical cancer in mice. The group has previously reported on the approach of treating tumors with viral etiologies as infectious disease using viral antigens as targets (*PLoS One.* 2007;2[10]:e1114). They hypothesized that pretreatment of tumor cells with various agents that cause cell death and/or elevation of E6 levels would increase accumulation of radiolabeled antibodies to E6 in cervical tumors. In the current study, human papilloma virus (HPV) type 16–positive CasKi cells were treated in vitro with up to 6 Gy of external radiation, with MG-132, or with unlabeled anti-E6 antibody C1P5. Cell death was assessed, as well as biodistribution of ^{188}Re-labeled C1P5 antibody in controls and radiation MG-132–treated tumor-bearing mice. The authors found that the radiolabeled antibody showed good tumor specificity, very low uptake, and fast clearance from major organs. Although tumor uptake was enhanced by MG-132, it was not affected by radiation pretreatment. In vitro studies showed that even unlabeled antibody caused cell death. They concluded that "pretreatment of cervical tumors with the proteasome inhibitor MG-132 and with unlabeled antibody to E6 can serve as a means to generate nonviable cancer cells and to elevate the levels of target oncoproteins in the cells for increasing the accumulation of targeted radiolabeled antibodies in tumors."

Cancer

PET in ^{90}Y RIT Assessment

In a study e-published on February 10 ahead of print in *Annals of Oncology*, Lopci et al. from University Hospital S. Orsola-Malpighi (Bologna, Italy) reported on a retrospective study of PET evaluation after radioimmunotherapy (RIT) with ^{90}Y-ibritumomab tiuxetan in patients with non-Hodgkin follicular lymphoma. Data included the records of 59 relapsed or refractory follicular lymphoma patients treated with RIT in 4 PET centers who underwent imaging before and after treatment. Posttreatment imaging indicated 45.8% complete responders, 25.4% partial responders, and 28.8% nonresponders (including both stable and progressive disease), with an overall survival of 71.2%. Over a median follow-up period of 23 mo, a statistically significant relationship was noted between disease extent before RIT and response to treatment in those with progression-free survival, but no other prognostic factors showed significant correlations. In multivariate analysis, post-RIT PET proved to be the sole independent predictor of progression-free survival.

Annals of Oncology

PET in Indeterminate Thyroid Nodule FNA Biopsy

Traugott et al. from the Washington University School of Medicine (St. Louis, MO) reported on February 6 ahead of print in the *World Journal of Surgery* on the use of ^{18}F-FDG PET to predict or exclude malignancy in patients with indeterminate fine-needle aspiration (FNA) biopsy cytology. This interim report from a large, ongoing prospective study included 51 patients, each of whom had a dominant thyroid nodule that was palpable or ≥1 cm in greatest dimension on ultrasound and whose FNA histologies were indeterminate. All participants underwent either preoperative neck PET or PET/CT. Image analyses were compared with histopathologic results after thyroidectomy. For all lesions (10 malignant, 41 benign), the sensitivity, specificity, and positive- and negative-predictive values for PET were 80%, 61%, 33%, and 93%, respectively. On pathologic analysis, 2 malignant and 6 benign lesions were found to be <1 cm, and 1 lesion was not measured. With these lesions excluded, the sensitivity, specificity, and positive- and negative-predictive values for PET were 100%, 59%, 36%, and 100%, respectively. The authors concluded that these preliminary data suggest that "FDG PET may have a role in excluding malignancy in thyroid nodules with an indeterminate FNA biopsy." The group plans to enroll a total of 125 participants in the study.

World Journal of Surgery

Thyroid Incidentaloma on PET

Ohba et al. from the Hamamatsu University School of Medicine (Japan) reported on February 17 ahead of print in the *Endocrine Journal* on a study designed to assess rates of cancer in focal thyroid incidentaloma discovered on ^{18}F-FDG PET imaging in otherwise healthy individuals. The 3-y study included a total of 1,501 healthy volunteers (mean age, 43.5 ± 9.7 y), in 20 of whom focal thyroid incidentalomas were discovered. When additional diagnostic studies indicated thyroid cancer, surgical resection was performed. Patients who did not undergo surgery were offered annual ultrasound and PET examinations, with fine-needle aspiration biopsy performed in the fourth year after the discovery of the incidentaloma. Final diagnoses in the 20 individuals with incidentalomas were malignant in 11 (10 papillary thyroid carcinoma, 1 thyroid carcinoma showing thymus-like differentiation), indeterminate in 1, and benign in 8. Seven patients not treated initially with surgery underwent annual PET imaging. One patient with papillary thyroid carcinoma showed increasing uptake over the monitoring period, but another with a benign nodule showed a similar increase. Five others showed negligible uptake changes, and these were found to be unrelated to status. The authors concluded that "focal thyroid PET incidentaloma in relatively young healthy adults has a high probability of malignancy" but that repeated PET "to follow up patients with thyroid nodules is ineffective."

Endocrine Journal

PET/CT in Recurrent Thyroid Carcinoma

Razfar et al. from the University of Pittsburgh Cancer Institute (PA) reported in the February issue of the *Archives of Otolaryngology–Head and Neck Surgery* (2010;136:120–125) on a retrospective study to determine the efficacy of PET/CT in identifying recurrent thyroid cancer and to elucidate its role in clinical management. The study included 124 patients with previously treated thyroid carcinoma who had undergone ^{131}I imaging before PET/CT. Of these, 80.6% had negative findings on ^{131}I imaging. PET/CT findings were positive in 75 and negative in 49 patients, with 71 true-positives and 32 true-negatives, yielding sensitivity, specificity, and positive- and negative-predictive values of 80.7%, 88.9%, 94.7%, and 65.3%, respectively. Significant differences were noted in mean serum thyroglobulin levels between patients with positive and negative PET/CT results. PET/CT detected distant metastases in 20.2% of patients, with changes in treatment plans for 28.2% of patients as a result of the incremental PET/CT data. More than 20% of patients underwent additional surgery. The authors concluded that "additional information from PET/CT in patients with ^{131}I-negative and thyroglobulin-positive tumors frequently guides the clinical management of recurrent thyroid carcinoma."

Archives of Otolaryngology–Head and Neck Surgery

PET in Retroperitoneal Fibrosis

In an article e-published on February 15 ahead of print in *Nephrology, Dialysis, Transplantation,* Piccoli et al. from the San Luigi Gonzaga University Hospital (Turin, Italy) reported on initial studies on the use of PET to detect retroperitoneal fibrosis (RF) and to resolve conventional imaging challenges in discriminating between types of lesions. The study included 7 patients (6 men, 1 woman; ages 41–79 y), in 3 of whom RF was associated with autoimmune disease and in 3 others with aortic aneurysm, with the remaining case characterized as idiopathic. Initial diagnoses were made by CT or MR, with PET imaging performed in all patients at referral and during follow-up. Treatments and management (including tamoxifen, steroid, and immunosuppressor administration and ureteral stent removal) were guided by PET findings on disease activity as well as individual side effects and tolerance. Only 1 relapse was recorded over 163 mo of follow-up (median, 24 mo) by PET. The authors concluded that "PET is a promising tool for surveillance of disease activity and for planning the removal of ureteral stents in RF."

Nephrology, Dialysis, Transplantation

^{201}Tl-Gated SPECT vs Echo in LVEF Assessment

Harpaz et al. from the E. Wolfson Medical Center (Holon, Israel) reported on February 2 ahead of print in *Clinical Cardiology* on a study comparing 2-dimensional echocardiography (2-DE) with ^{201}Tl-gated SPECT in assessment of left ventricular ejection fraction (LVEF). The study included 402 patients, all of whom underwent ^{201}Tl-gated SPECT in the same laboratory and then underwent 2-DE in either a tertiary hospital or a community laboratory. LVEF evaluations were similar between SPECT and 2-DE, regardless of the site at which 2-DE was performed. Because patients who underwent in-hospital 2-DE had higher rates of past myocardial infarction than the community group (46.7% and 22.2%, respectively), the latter group had higher average LVEFs, reflected in both types of imaging. The authors concluded that because "^{201}Tl-gated SPECT is a reliable clinical tool for LVEF assessment, with good correlation when compared to 2-DE" it may be "routinely used as an alternative for patients with poor acoustic visualization and should be performed systematically in patients undergoing myocardial perfusion imaging with ^{201}Tl."

Clinical Cardiology

SPECT/CT in Knee Arthroplasty

Hirschmann et al. from the Kantonsspital Bruderholz (Switzerland) reported on February 11 ahead of print in *Knee Surgery, Sports Traumatology, Arthroscopy* on a novel standardized SPECT/CT algorithm for clinical evaluation of patients with painful total knee arthroplasty (TKA). The SPECT/CT localization scheme, which included 9 tibial, 9 femoral, and 4 patellar regions on standardized axial, coronal, and sagittal slices, was used in 18 patients with post-TKA pain. Tracer activity was recorded using a color-coded scale (0–10). The localization scheme was found to have high inter- and intraobserver reliability in all regions. The median interobserver difference between alignment measurements for tibial and femoral components was $<3°$, and median intraobserver variability for these measurements was $<2°$. Biometrics (calculated measurements of component positions) were highly reliable in all cases, with sufficient visibility of anatomical landmarks. The authors concluded that this approach is both reliable and useful in management of patients with painful TKA and, because it combines biomechanical and metabolic data, provides "an extra dimension to the understanding of this difficult condition."

Knee Surgery, Sports Traumatology, Arthroscopy

Metabolic Syndrome and Stress Testing

In an article e-published on February 15 ahead of print in *Metabolic Syndrome and Related Disorders,* Kamalesh et al. from Indiana University (Indianapolis) reported on a study of the relationship between metabolic syndrome and risk of coronary disease in individuals with traditional risk factors referred for stress imaging. The study began with 2,626 individuals who underwent clinically indicated stress imaging studies using echocardiography or SPECT myocardial perfusion. Patients (n = 1,370) with known coronary artery disease (CAD) were excluded, leaving 1,256 participants. Metabolic syndrome, as defined by the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) criteria, was identified in 540 (43%) of these participants. The authors assessed the effect of metabolic syndrome on CAD prevalence in those with limited ($\leq$2) and those with multiple ($>$2) traditional risk factors. The presence of metabolic syndrome was found to be associated with a nonsignificant 3%−4% increase in overall prevalence of CAD and did not increase the prevalence of CAD in either the multiple traditional risk factor or limited risk factor group. None of the 5 individual components of metabolic syndrome showed significant association with CAD.

Metabolic Syndrome and Related Disorders

REVIEWS

Review articles provide an important way to stay up to date on the latest topics and approaches and provide valuable summaries of pertinent literature. The Newsline editor recommends several reviews accessioned into the PubMed database in late January and February. These include "Imaging of cell trafficking in Crohn's disease" by Glaudemans et al. from the University Medical Center Groningen (The Netherlands), e-published on February 19 ahead of print in the *Journal of Cell Physiology*; "Combining nanotechnology with current biomedical knowledge for the vascular imaging and treatment of atherosclerosis" by Slevin et al. from Manchester Metropolitan University (UK) in the March issue of *Molecular Biosystems* (2010;6:444–450); "Thyroid incidentalomas: to treat or not to treat" by Iyer et al. from the Memorial Sloan–Kettering Cancer Center (New York, NY), e-published on February 13 ahead of print in the *European Archives of Oto-rhino-laryngology*; and 3 related articles e-published in the January 26 issue of *Current Pharmaceutical Design*: "Clinical PET imaging of insulinoma and β-cell hyperplasia" by Kauhanen et al. from the University of Turku (Finland); "Development of radiotracers for the determination of the β-cell mass in vivo" by Brom et al. from the Radboud University Nijmegen Medical Center (The Netherlands); and "Identification of new pancreatic β-cell targets for in vivo imaging by a systems biology approach" by Bouckenooghe et al. from the Université Libre de Bruxelles (Belgium).