9. Gygi SP, Rochon Y, Franza BR, Aebersold R. Correlation between protein and mRNA abundance in yeast. *Mol Cell Biol.* 1999;19:1720–1730.
10. Celis JE, Gromov P. Proteomics in translational cancer research: toward an integrated approach. *Cancer Cell.* 2003;3:9–15.
11. Hunter T. Signaling: 2000 and beyond. *Cell.* 2000;100:113–127.
12. Macbeath G. Protein microarrays and proteomics. *Nat Genet.* 2002;32(suppl): 526–532.
13. Liotta LA, Espina V, Mehta AI, et al. Protein microarrays: meeting analytical challenges for clinical applications. *Cancer Cell.* 2003;3:317–325.
14. Paweletz CP, Charboneau L, Bichsel VE, et al. Reverse phase protein microarrays which capture disease progression show activation of pro-survival pathways at the cancer invasion front. *Oncogene.* 2001;20:1981–1989.
15. Deutsch EW, Eng JK, Zhang H, et al. Human Plasma Peptide Atlas. *Proteomics.* 2005;5:3497–3500.

David Geho, MD, PhD
Research Professor
Center for Applied Proteomics and Molecular Medicine
George Mason University
Manassas, VA

Recent Trends in Radionuclide-Based Molecular Imaging

Radionuclide-based molecular imaging can utilize nuclides with varying decay properties and half-lives. Although significant interest focuses on the application of SPECT in molecular imaging, the major advances over the past several years have utilized PET. Several factors explain this trend, including:

(1) The availability of a wide variety of radiopharmaceuticals labeled with positron-emitting radionuclides that can be used to study molecular function in a whole variety of diseases. These include: cancer, cardiac disease, pulmonary disease, infection, and inflammation.
(2) The ability to obtain truly quantitative data utilizing PET imaging. Although techniques to quantify SPECT images have improved over the past several years, the ability to obtain truly quantitative data with PET is an advantage.
(3) Modern SPECT instrumentation, both for animal and human studies, has improved in resolution over the past several years. This achievement, however, has been made with a corresponding sacrifice in sensitivity. The higher sensitivity of PET imaging allows greater use of dynamic imaging and the ability to obtain quantitative metabolic and other functional parameters.
(4) The ability to obtain very high specific-activity radionuclides and, hence, radionuclide-based molecular imaging probes allows (in principle) the rapid translation of radionuclide-based molecular imaging from concept to animal studies to patient studies. This has allowed the investigation of such parameters as neuroreceptor imaging, measurements of quantitative cardiac metabolism, tumor metabolism and receptors, as well as other parameters, such as the efficacy of gene therapy. Other techniques under investigation include those to monitor trafficking of specific groups of separated cells.

Issues remain to be addressed in radionuclide-based imaging techniques. Among these are questions related to coregistration. The development of combined PET/CT scanners has allowed major expansion of molecular imaging utilizing 2-fluoro-2-deoxyglucose (^{18}F-FDG) for tumor imaging. The addition of CT to PET, however, produces an increased radiation dose. In animal imaging, where research has been carried out on combined PET/CT scanners and combined SPECT/CT, the radiation dose is significant. The development of a truly integrated MR/PET scanner would be a tremendous advantage.

Although research groups have described radiopharmaceuticals to measure many of the parameters discussed here, more than 90% of human PET studies involve a single tracer: ^{18}F-FDG. New agents face significant barriers in translating to clinical use. These barriers include but are not limited to:

(1) Intellectual property. A significant number of promising radiopharmaceuticals are not patent protected. It is unlikely that a commercial company will invest significant funds to translate these agents to the clinic.
(2) Although many regional radiopharmacies now produce ^{18}F-FDG, many of the other positron-emitting radiopharmaceuticals under investigation have low radiochemical yield. This makes the commercial applicability of these somewhat limited. With the current funding levels at the National Institutes of Health, it is unlikely that funding can be obtained to simply increase the radiochemical yield of a validated radiopharmaceutical.
(3) Although the requirements for Investigational New Drug Applications by the U.S. Food and Drug Administration have been simplified, human use approval of new radioactive probes is still perceived as a roadblock.

Michael J. Welch, PhD
Co-Director, Division of Radiological Sciences
Washington University School of Medicine
Mallinckrodt Institute of Radiology
St. Louis, MO