Realizing the Full Potential of PET for Measuring the Biodistribution of Novel Anticancer Agents

TO THE EDITOR: The unique specificity and sensitivity of PET offers a means to support the development of new anticancer agents. Radiolabeling of a drug with ^{11}C or ^{18}F allows PET measurement of drug biodistribution to be undertaken at the microdose and therapeutic dose level (*1–3*). An example is targeted agents such as antisense oligonucleotides, for which in vivo biodistribution was first reported using PET in primates in 1998 (*4*).

Since this groundbreaking work in PET-based molecular imaging, there have been few follow-up studies on human cancer patients. However, a recent report on the use of an ^{11}C-labeled second-generation antisense oligonucleotide to survivin (*5*) demonstrated the power of the PET technology for theranostics drug development (*6*). Not only was the biodistribution of the novel agent shown, but an important dose effect was demonstrated, with implications on how such an agent is administered to patients (*6*).

This latest study highlights several important questions on how PET-based molecular imaging can affect cancer theranostics drug development in the future:

- Why has it taken so long to translate from the earlier pioneering preclinical work in PET to human studies?
- Why are more studies not being undertaken?
- Why has PET underachieved in making an impact on cancer drug development and theranostics, to which it potentially can make a major unique contribution?
- Can these studies be undertaken only within the expensive and complex facilities of "big science PET centers," resulting in the study of fewer than ideal numbers of patients?
- Why are studies not undertaken in specialized oncology departments, where important contributions and proposals for clinical experimental studies arise?

We believe the answers to these challenging questions rest on the fact that the advanced technology required is too complex and expensive for leading clinical researchers to access easily or productively. There is still insufficient access to the generic radiolabeling methodologies available to exploit the wealth of opportunities for PET studies of biologic macromolecules. A paradigm shift in drug development, to bring PET into mainstream clinical translational research and to enhance chemistry and biology support, is also clearly required. We write to draw your readers' attention to potential solutions: the development and availability of low-cost, low–radiation-emitting, simple-to-operate positron-emitting radioisotope generators and of inexpensive disposable, good-manufacturing-practice–compliant "card-based" radiosynthesis platforms that lighten regulatory overload (*7*). These systems should be used to implement generic radiolabeling procedures, such as those reported for peptides and proteins (*8*) and oligonucleotides (*9*). We hope the development of these new technologies is encouraged by others in the molecular imaging community.

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