the enzymatic approach is that in principle no enzymes are required to cleave these kinds of bonds.

I share the authors' view that intracellular metabolism can very well be studied in in vitro model systems; however, it should be noted that in vitro procedures may suffer from limitations like decreased enzyme activity of cell-homogenates and lysosomal lysates. These can be caused by isolation artefacts, like loss of co-factors during the work-up of these preparations. Therefore, a combination of in vitro and in vivo studies are needed to obtain optimal results on the intracellular metabolism of receptor-targeted proteins. Finally, the identification of metabolites like ^{111}In-DTPA-lysine contributes to the understanding why high background radioactivity of labeled monoclonal antibodies is observed in the liver and kidneys. Improved knowledge on this point aids in the rational design of improved drug/nuclide targeting preparations.

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E.J.F. Franssen
University Hospital Groningen
Groningen, the Netherlands

REPLY: We appreciate Dr. Franssen's interest and insightful comments. We agree entirely with the central theme of his letter: an understanding of intracellular metabolism will be key in the rational design of targeted drugs and diagnostic agents. We also agree with his contention that derivatization of the ϵ-amino group of lysine does not prevent lysosomal efflux of lysine derivatives per se. Rather, we suggested that ^{111}In-DTPA-amino acids would remain within the lysosome since their positive and negative charges would limit diffusion across the membrane (*1*). We also believe that size, charge and lipophilicity of the drug or nuclide-chelator will determine lysosomal efflux properties. When identifying in vivo metabolites, we found the predominant metabolite was ^{111}In-DTPA-ϵ-lysine and only small amounts of ^{111}In-DTPA were produced (*2*). We were pleased to find Dr. Franssen's work, as well as other reports that suggest that lysosomes infrequently hydrolyze the amide bonds between lysine and "foreign" substances such as drugs and chelates.

We also hope to modulate the rates of lysosomal efflux through appropriate choices of chelates and their linkages to protein backbones. We plan to test these using reconstituted systems, cell culture models and in vivo experiments.

In summary, we hope all our correspondence with this journal will be in the same tone of complete agreement.

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James R. Duncan
Michael J. Welch
F. Nicholas Franano
Mallinckrodt Institute of Radiology
Washington University Medical Center
St. Louis, Missouri

TBI Is Not MIBI

TO THE EDITOR: I read with great interest the case report by Desai and Yuille describing ^{99m}Tc-MIBI uptake in a recurrent carcinoid tumor (*1*). Three ^{99m}Tc-labeled isonitriles have been evaluated in detail in humans: TBI (tertiarybutyl isonitrile), CPI (carbomethoxyl isopropyl isonitrile) and MIBI (methoxy isobutyl isonitrile) (*2–4*). High uptake in the lung and liver limited the clinical use of ^{99m}Tc-TBI (*2,5–7*). However, ^{99m}Tc-MIBI, an ether-substituted analog of ^{99m}Tc-TBI, has gained wide clinical acceptance.

Desai and Yuille stated that Ramanathan et al. (*8*) had used ^{99m}Tc-MIBI for visualization of suppressed thyroid tissue, confusing TBI with MIBI. In fact, Ramanathan et al. have used ^{99m}Tc-TBI for this purpose. Although both ^{99m}Tc-MIBI and ^{99m}Tc-TBI are essentially isonitriles, they have different chemical structures, biological behavior and in vivo distribution (*2,5–11*).

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