Letters to the Editor

Therapeutic potential of epidermal growth factor receptor–related protein

In Response:

We respectfully disagree with some of the issues raised by Reiter et al. that imply that epidermal growth factor receptor–related protein (ERRP) lacks therapeutic value. Our studies show the pan-erbB inhibitory nature of ERRP, which inhibits the growth of human colon- and pancreatic cell-derived tumors (1, 2).

Although the genetic identity of human ERRP is not known, reverse transcription-PCR analyses indicate that the rat ERRP transcript is a 'chimera' formed with EGFR and peptidase D mRNAs (2). The region of ERRP mRNA corresponding to EGFR encodes a polypeptide containing three of the four ectodomains of EGFR. The peptidase D part of the rat ERRP mRNA does not encode peptidase D protein due to a 29-nucleotide insertion at the junction of the EGFR and peptidase D sequences. As a consequence, a frameshift occurs in the peptidase D sequence that results in the presence of 27 new amino acids (termed the 'U' region) at the COOH-terminus of ERRP.

The ability of rat ERRP to induce a host antigenic response was examined by analyzing CD69 expression in human peripheral blood lymphocytes in response to recombinant ERRP *in vitro* (2). CD69 is a member of the natural killer cell gene complex family of signal transducing receptors. Although not expressed in resting lymphocytes, CD69 represents the earliest activation marker, being rapidly induced on the cell surface on stimulation. CD69 expression is thought to be a useful early marker of antigen- or allergen-specific activation of lymphocytes. We observed that whereas concanavalin-A elevated CD69 expression by ~33%, recombinant ERRP caused <10% increase compared to the controls (2). The latter increase is thought to be typical of marginal activation, suggesting that ERRP is unlikely to induce aggressive immunologic responses. We also observed that in non–tumor-bearing severe combined immunodeficient mice, recombinant ERRP up to 4 mg/kg produced no signs of toxicity. Thus, we believe that regardless of the genetic identity of ERRP, our studies have provided good evidence that ERRP is an effective pan-erbB inhibitor and therefore remains a potential anticancer agent.

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References

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Mol Cancer Ther 2006;5(11):2955

doi:10.1158/1535-7163.MCT-06-0120

Molecular Cancer Therapeutics

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Mol Cancer Ther 2006;5:2955.