HUMAN TUMOR STEM-CELL ASSAY

To the Editor: Since our group first reported on the potential clinical applications of the human tumor stem-cell, or clonogenic, assay in the journal, we think some comment from us is warranted regarding the recent article by Selby et al. and the editorial by Von Hoff. We clearly agree that it is important to plate good single-cell suspensions, that drug-sensitivity criteria are still in the developmental stages, that some drugs may require the evaluation of various exposure times, that inappropriate drug concentrations may be misleading, that drugs requiring bioactivation present special problems, that radiation-survival curves with plateaus at high dosage probably represent artifacts, that individual tumor types need special effort in assay development, and that clinical-response criteria, such as the partial response, may not translate into a survival advantage. All these factors are subjects of ongoing research. Complete remission, prolonged survival, and cure will eventually prove to be better benchmarks for clinical correlation of drug effects in vitro. A recent review of clinical evaluations in over 450 patients studied in various institutions supports the clinical potential of chemosensitivity testing in certain types of tumor and documents that the assay can identify chemosensitive patients. We don’t think that the assay system is ready for routine clinical use. Currently, its application to ovarian cancer in relapse appears particularly promising. However, clonogenic assay procedures cannot be expected to improve the clinical response to drugs markedly as long as available drugs are relatively ineffective.

Principally, on the basis of theoretical constructs, Selby et al. provided their perspectives on clonal assays, assuming a hierarchical model of tumor stem-cell differentiation. This model will also require critical testing and clinical correlation.

We agree with Von Hoff that research on tumor cloning obviously should be viewed as evolutionary rather than as a completed construct requiring immediate acceptance or rejection. The scope of research involving in vitro studies of human tumors and investigations of their applicability to chemosensitivity testing is greater now than we would have predicted at the time of the first report in the journal five years ago.

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