Tumor heterogeneity revealed by drug-induced apoptosis (MiCK) assays in lung cancer.

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Author(s):
Dennis A. Wigle, Cary A. Presant, Allan Hallquist, Mathieu Perree, James Rutledge, Julian R. Molina; Mayo Clinic, Rochester, MN; Wilshire Oncology Medical Group, US Oncology, La Verne, CA; DiaTech Oncology, Montreal, QC, Canada; Diatech Oncology, Brentwood, TN; Data Vision, Miami, FL

Background: Evidence suggests that drug-induced apoptosis testing may facilitate individualized chemotherapeutic regimens, and may correlate with patient survival when using the MiCK assay (Cancer Res 2012; 72: 3901). Given recent demonstrations of tumor heterogeneity from genome sequencing, we explored inter-tumoral heterogeneity for tumors sampled from different sites with the MiCK assay.

Methods: Patients with non-small cell lung cancer (NSCLC) or mesothelioma had tumors from different sites sent independently for drug-induced apoptosis testing. Purified tumor cells were cultured for 48 hours with individual drugs, and apoptosis was measured optically using light-scattering. Results from paired tumor sites in individual patients were compared and analyzed statistically. Active apoptosis (sensitivity) was defined as >= 1.0 kinetic units (KU), and no apoptosis (resistance) was < 1.0 KU, and 2 standard deviations (SD) in the assay were 1.14 KU.

Results: 10 paired specimens were obtained from 5 NSCLC pts and 1 mesothelioma pt. The mean number of individual drug apoptosis tests analyzed per pt was 20.6 (range 3 to 39). There was concordance (within 2 SD) of drug-induced apoptosis in 97/103 assays (94%; 95% confidence interval [CI] 84% - 100%). Paired specimens analyzed for sensitivity or resistance showed concordance (within 2 SD) in 95% of assays (CI 85% - 100%). The best chemotherapy from specimen A was also shown to be the best chemotherapy from specimen B (within 2 SD) in 72% of 57 best drug assays (CI 36% – 100%). The best chemotherapy from specimen B was identical to the best chemotherapy for specimen A in 58% of 71 best drug assays (CI 27% – 89%).

Conclusions: Significant inter-tumoral heterogeneity is not present in individual paired measurements of drug-induced apoptosis in the MiCK assay for lung cancer. However, since in 28% to 42% of assays the best chemotherapy from one site is not the same as best chemotherapy from an alternate site, analysis of multiple specimens may be appropriate in individual patients. Selection of metastases for apoptosis assays may be more desirable. In NSCLC, the DiaTech MiCK assay may identify chemotherapy regimens which produce the highest apoptosis.