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Detecting Attomolar DNA-Damaging Anticancer Drug Activity in Cell Lysates with Electrochemical DNA Devices ASHAN WETTASINGHE, JASON SLINKER, University of Texas at Dallas — This work, we utilize DNA-based electrochemical devices to quantitatively follow drug-induced DNA damage from the catalytic biochemical reaction of an experimental drug under clinical trials, isobutyl-deoxynyboquinone (IB-DNQ). These measurements are performed directly in lysates of cancer and control cells, and the cancer-selective DNA-damaging nature of these drugs is confirmed. Under cancerous conditions, we observed a limit of detection of IB-DNQ of a mere 380 aM (57000 molecules) and high selectivity over the control. While this speaks to the high sensitivity of these biosensing devices, this low limit was surprising given the lethal concentration (LC_{50}) of 110 nM in cell survival assays and similar activity thresholds in other cell experiments. This discrepancy led to a key observation of the biotechnology: our measurement technique does not require cellular uptake of the drug, permitting us to see its inherent potential for DNA damage. The rate of DNA damage on our chip surface matched that found in the cell survival assay (Hill coefficients, NQO1+). Ultimately, these results speak to the noteworthy potency and selectivity of IB-DNQ and the high sensitivity and precision of electrochemical DNA devices to analyze agents/drugs involved in DNA-damaging immunotherapies.

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