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An Assay for HIV RNA in Crude Infected Cell Lysates, and Its Use for the Rapid Evaluation of Antiviral Efficacy, L. Bacheler*, M. Paul*, M. J. Otto*, P. K. Jadhav*, B. A. Stone†, and J. A. Miller†. Viral Diseases Research* and Nucleic Acid Technology†, Research and Development Division, Du Pont Merck, Experimental Station, Wilmington, DE. 19880-0400

A rapid, high capacity assay for evaluating the potency of anti-HIV compounds was devised based on measuring cell associated viral RNA levels three days after infection of susceptible T cell lines grown in individual microtiter plate wells. Levels of cell associated viral RNA were shown to correlate with those of infectious virus, and formed the basis of the test. Viral RNA was detected by a sandwich hybridization assay, the first step of which was performed directly in crude infected cell lysates prepared in guanidinium isothiocyanate. Antiviral potencies of a large series of compounds tested in this RNA hybridization assay correlated closely with potency values determined by a sensitive but slower and more labor intensive yield reduction assay. Both laboratory strains and selected clinical isolates of HIV can be detected in this RNA hybridization assay.

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The Discovery and General SAR Studies of a Novel Class of Potent Non-Nucleoside Reverse Transcriptase Inhibitors. R. J. Ternansky[1], J. M. Morin, Jr.[1], C. Lopez[1], C. J. Paget, Jr.[1], F. W. Bell[1], A. S. Cantrell[1], S. R. Jaskunas[1], C. L. Jordan[1], M. D. Kinnick[1], J. A. Palkowitz[1], C. A. Parrish[1], P. Pranc[1], R. T. Vasileff[1], S. J. West[1], M. Hogberg[2], P. Lind[2], R. Noreen[2], C. Sahlberg[2], X.-X. Zhou[2], L. Vrang[2], C. Rydergard[2], C. Ahgren[2], B. Oberg[2], and N. G. Johansson[2].

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As part of an ongoing collaborations between the Lilly Research Laboratories and Medivir AB, a new class of non-nucleoside inhibitors of reverse transcriptase was discovered. The lead compound in the series, LY73497, inhibits HIV-1 in MT4 cells with ED_{50} of 0.35 μg/ml. The 50% cytotoxic doses in MT-4 cells is >100 μg/ml. The SAR of the lead compound was performed by dividing this derivative into four sections and independently varying substituents in each quadrant. This poster will describe rationale for the discovery of LY73497 and the basic structure-activity relationships for this new series of compounds.