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PRELIMINARY CHARACTERIZATION OF APOBEC3G DNA DEAMINASE INHIBITORS IDENTIFIED BY HIGH THROUGHPUT SCREENING

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The human APOBEC3G (A3G) protein is a DNA deaminase that has potent activity against HIV-1 and a variety of other retroelements. The role of A3G deaminase activity in HIV-1 restriction and HIV-1 drug resistance is still in debate partly due to the lack of specific small molecule inhibitors. A *bona fide* A3G deaminase inhibitor would be a useful chemical probe for a wide variety of *in vitro* and *in vivo* studies.

To identify A3G inhibitors, we have developed, optimized and miniaturized a fluorescence-based single-strand DNA (ssDNA) deaminase assay. We have used this assay in a preliminary high throughput screen of the Library of Pharmacologically Active Compounds (LOPAC) in collaboration with the Institute for Therapeutics Discovery and Development (ITDD) at the University of Minnesota. A small screen of 1280 compounds yielded 46 candidate actives. For a subset of these lead molecules, we will present kinetic data, specificity studies and nuclear magnetic resonance spectroscopy binding data.