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(54) Title: DISRUPTION OF THE PROCESSING OF THE VIRAL CAPSID-SPACER PEPTIDE 1 PROTEIN

(57) Abstract: Inhibition of HIV-1 replication by disrupting the processing of the viral Gag capsid (CA) protein (p24) from the CA-spacer peptide 1 (SP1) protein precursor (p25) is disclosed. Amino acid sequences containing a mutation in the Gag p25 protein, with the mutation resulting in a decrease in the inhibition of processing of p25 to p24 by dimethylsuccinyl betulinic acid or dimethylsuccinyl betulin, polynucleotides encoding such mutated sequences and antibodies that selectively bind such mutated sequences are also included. Methods of inhibiting, inhibitory compounds and methods of discovering inhibitory compounds that target proteolytic processing of the HIV Gag protein are included. In one embodiment, such compounds inhibit the interaction of the HIV protease enzyme with Gag by binding to Gag rather than to the protease enzyme. In another embodiment, viruses or recombinant proteins that contain mutations in the region of the Gag proteolytic cleavage site can be used in screening assays to identify compounds that target proteolytic processing.

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