Oral Session III

Retrovirus Infections – Part II

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Three-dimensional structure of a ternary complex of human immunodeficiency virus-1 reverse transcriptase, a monoclonal antibody Fab fragment, and double-stranded DNA.

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Using recombinant HIV-1 RT p66/p51 expressed in and purified from *E. coli*, we have obtained crystals of the heterodimer itself, and in complex with dsDNA primer-template mimics and with monoclonal antibody Fab fragments. We are pursuing structure determination of crystals of a ternary complex of HIV-1 RT p66/p51 heterodimer, the Fab fragment of a monoclonal antibody (previously designated 28), and dsDNA oligomers. These crystals diffract X-rays to 4 Å resolution without DNA present, but diffract to 3.1 Å resolution when either cocrystallized with or soaked with dsDNA oligomers.

We have recently obtained a low resolution structure of HIV-1 RT from an electron density map computed using five heavy atom derivatives at 7 Å resolution. We have complete data to 3.5 Å resolution and are pursuing the structure determination at high resolution. Preliminary experiments indicate the presence of ordered DNA in the crystals. These crystals of HIV-1 RT should be especially relevant for visualization of antiviral agent complexes with the enzyme. Knowledge gained from experimental determination of complexes with different classes of RT inhibitors may contribute to the development of better treatments for AIDS.