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The long-term objectives of this proposal are to develop and clinically test novel approaches for early detection and intervention in HIV infection. This project, the first of its kind, will test the hypothesis that treatment with antiretroviral drugs during primary infection alters early events that establish the HIV reservoir. Use of this method might enhance the effectiveness of antiretroviral therapy in reducing the size of the viral reservoir by interrupting the critical earliest events in the establishment of this pool of virus. The proposed experiments are relevant not only to the treatment of HIV infection but also to the treatment of infection with other viruses. The Specific Aims are: 1. To evaluate and characterize the effects of early treatment with antiretroviral therapy in SIV infection of macaques. Our recent studies in macaques have demonstrated that early treatment with antiretroviral drugs prevents both an early and a sustained setpoint viremia after infection. These data suggest that these agents might not only have a therapeutic role in the treatment of HIV infection but that they might also interrupt critical early events in the establishment of HIV latency. These studies will determine the effect of early treatment on the size and number of SIV-infected cells in peripheral blood, bone marrow and lymph nodes. 2. To determine the effect of antiretroviral therapy during primary infection in humans on the size and structure of the viral reservoir. Many individuals with HIV infection are unable to receive early treatment with antiretroviral drugs, although this therapy is clearly indicated for HIV-infected infants. The design of these studies will allow us to examine the effect of early treatment on the population structure of the viral reservoir. Such an investigation could clarify whether early treatment with antiretroviral drugs would reduce the size of the viral reservoir, making it more likely that ongoing therapy during primary infection would reduce the size of the reservoir. In these studies we will evaluate a large number of infants and children who are diagnosed with acute HIV infection. Children will be treated with antiretroviral drugs for their initial infection. We will follow these children longitudinally and

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