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Poster presentation

Cell specific temporal infection of the central nervous system in a simian immunodeficiency virus model of human immunodeficiency virus encephalitis

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Increasing evidence supports early central nervous system (CNS) infection by human immunodeficiency virus (HIV) and subsequent establishment of a brain viral reservoir. Definitive temporal studies determining when and within which CNS cells viral DNA is present are lacking. This study utilized simian immunodeficiency virus (SIV) infected macaques sacrificed at days 10, 21, 56 and 84 post-inoculation. Laser microdissection isolated pure perivascular macrophage, parenchymal microglia and astrocyte populations. Nested PCR and sequencing determined the presence and characteristics of SIV *env* V3 and V1 DNA from each population.

At day 10 viral DNA was detected in perivascular macrophages and astrocytes but not parenchymal microglia. gp41 expression was restricted to perivascular macrophages. At day 21, viral DNA was not detected in any cell type. At day 56, viral DNA was detectable in perivascular macrophages from one of two macaques, with no gp41 expression detected. At day 84 (morphologic and clinical encephalitis) viral DNA was detected in all cell types, gp41 was only detected in perivascular macrophages and parenchymal microglia. The neurovirulent molecular clone, SIV/17E-Fr, was the only genotype identified in the brain cell populations.

Early, productive brain SIV infection is transient and restricted to trafficking perivascular macrophage. No CNS reservoir was detected during subsequent asymptomatic disease. SIV later re-enters the CNS via infected perivascular macrophages and productively infects macrophages and parenchymal microglia. These data challenge current notions of an HIV reservoir in latently infected, semi-permanent brain cells and has significant implications for the timing and design of therapies to prevent primary HIV CNS diseases.