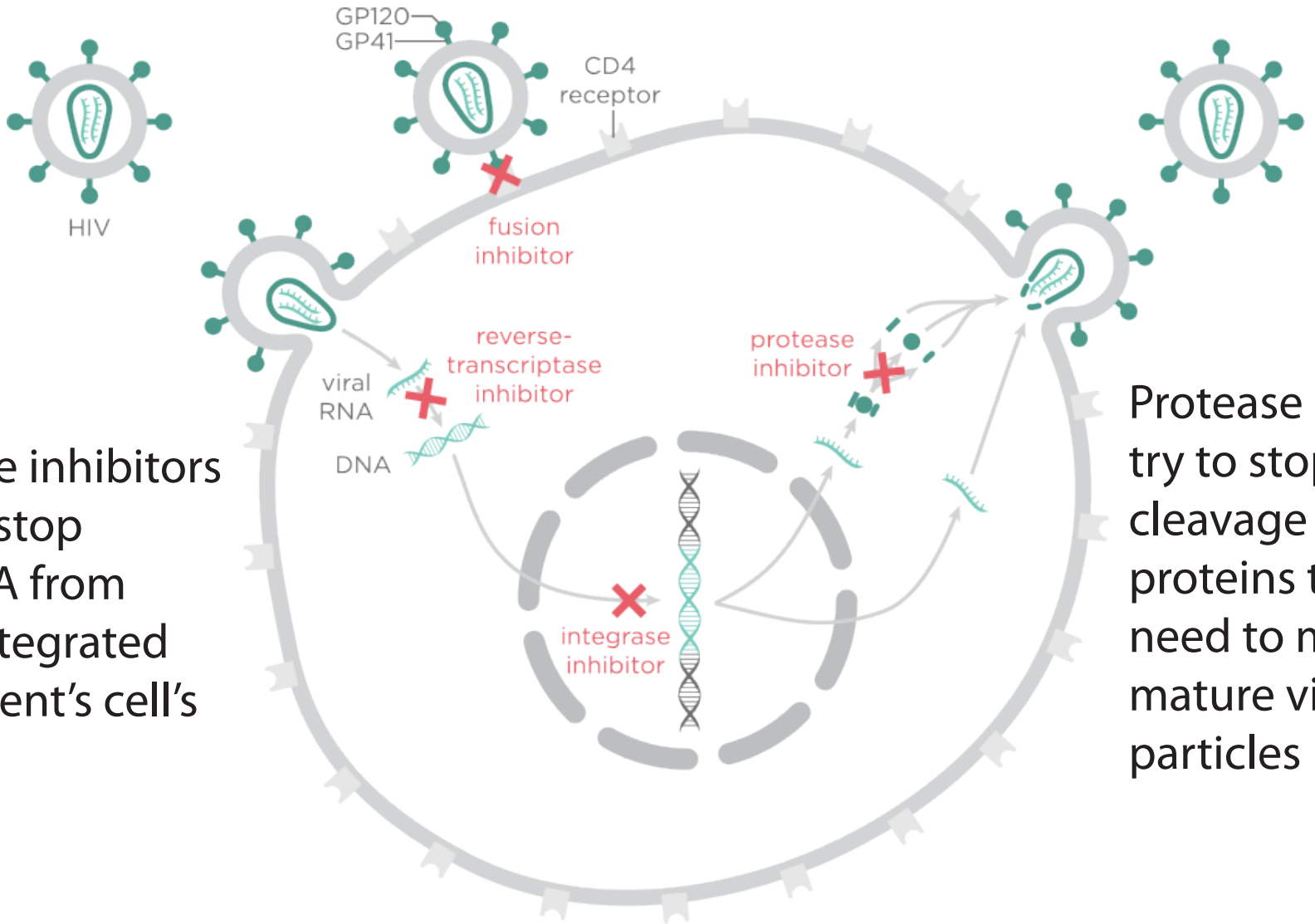
HAART ("Highly Active Antiretroviral Therapy") entails using multiple drugs to combat HIV infection.

Drugs that are used in HAART typically work by inhibiting one of the red-colored steps show below...



Integrase inhibitors work to stop viral DNA from being integrated into patient's cell's DNA

Protease Inhibitors try to stop cleavage of viral proteins that is need to make mature viral particles

above figure from Wikipedia entry on "HAART"

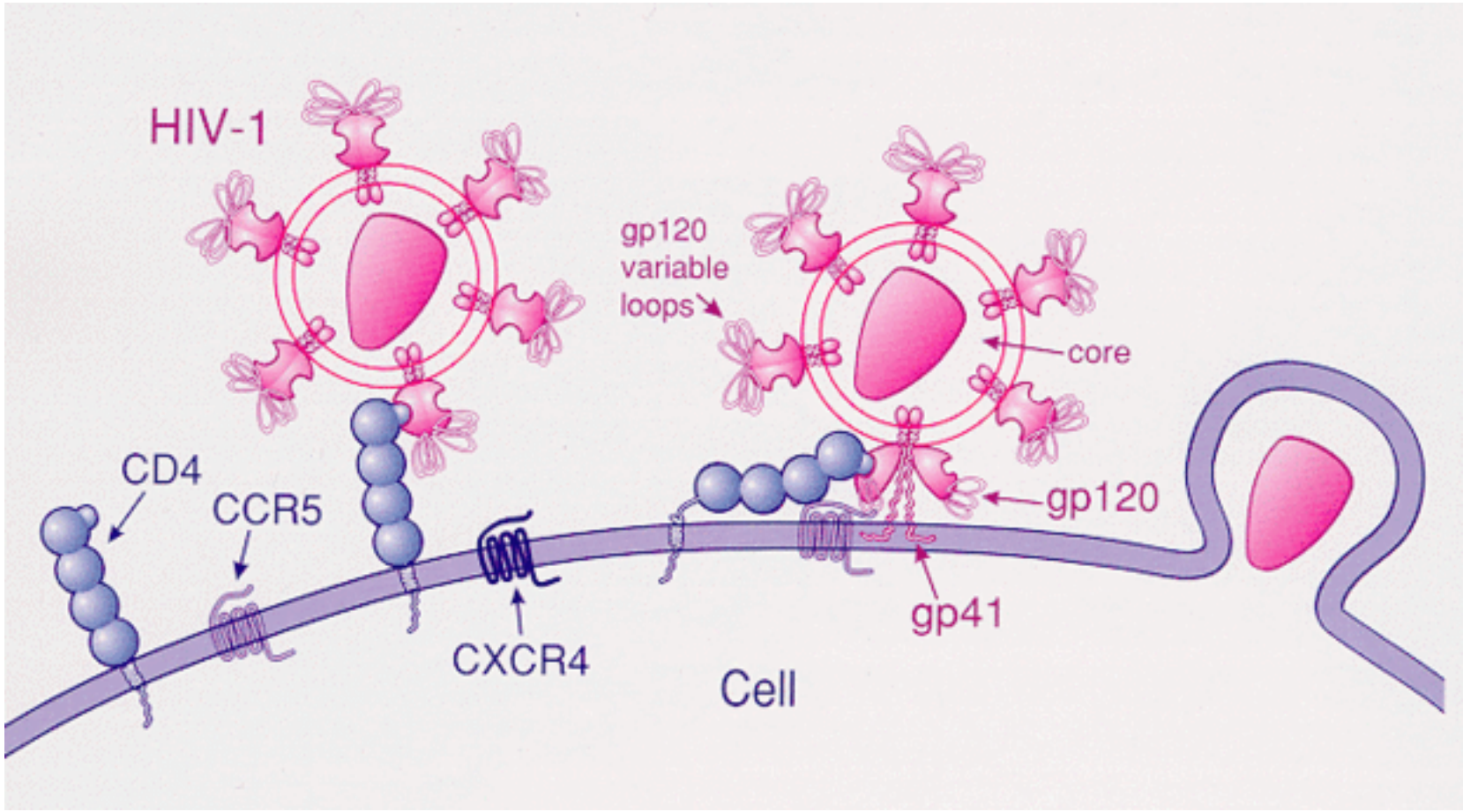
HIV infections are now "managed"

	Past	Present	Future
Epidemiology	Exponential increase in new infections Disease affects mainly young adults and children Disproportionate burden of new infections in high-risk* populations Life expectancy of less than 2 years after AIDS illness Low proportion of people with access to chronic ART	Fewer new adult infections, but more people living with HIV Disease increasingly common in middle-aged people Reduced number of HIV-infected children; more HIV-exposed uninfected children Disproportionate burden of new infections in high-risk* populations Greater proportion of people treated with ART Life expectancy of decades in treated patients	Few new HIV infections Elimination of HIV infection in children Disease spans age spectrum, with growing burden of disease in geriatric populations More HIV-infected but cured people Few AIDS-related deaths
Immune profile	Severe immune deficiency in untreated patients Partially restored immune deficiency in treated patients	Partially restored immune deficiency with ART Persistent inflammation contributing to incomplete health restoration	Restored immune function through earlier initiation of ART; anti-inflammatory interventions and functional cure in some patients
Disease burden	AIDS-defining illnesses and tuberculosis ART toxicity from early ART combinations	Decreasing AIDS-defining illness with residual persistent tuberculosis risk in ART-treated patients Increasing importance of cardiovascular, liver, renal, and cognitive complications of HIV	Morbidity reflecting age, as seen in HIV-uninfected general population No increased risk for tuberculosis
Health system	Hospital-based detection and care for symptomatic patients	Clinic and hospital based Move towards integrated HIV care cascade	Community-based and clinic-based integrated HIV care model, with specialty HIV cure services

ART=antiretroviral therapy. *Men having sex with men, transgender people, sex workers, injection drug users.

Table 1: **HIV as a chronic disease**

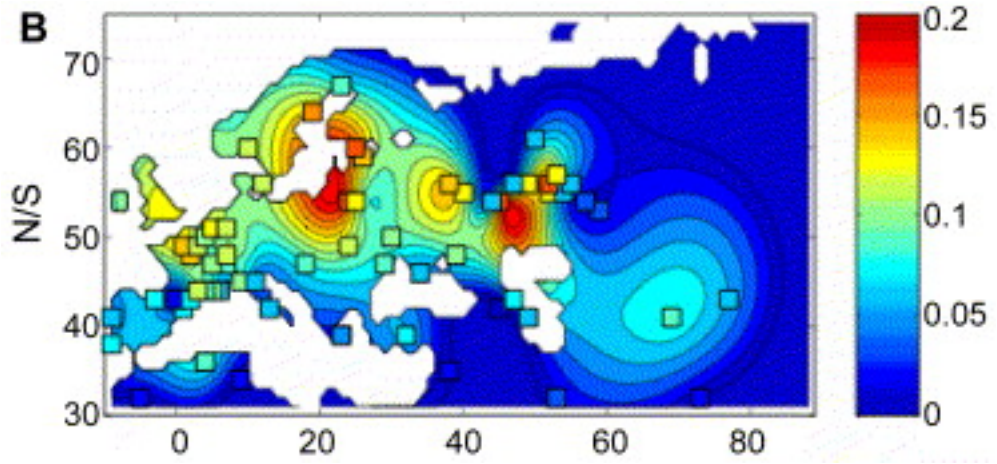
above is Table 1 from "The End of Aids: HIV as a chronic disease" by Deeks et al. 2013 Lancet 382: 1525-1533



"Attachment of HIV to a CD4+ T-helper cell: 1) the gp120 viral protein attaches to CD4. 2) gp120 variable loop attaches to a coreceptor, either CCR5 or CXCR4. 3) HIV enters the cell. "

taken from wikipedia entry on CCR5

Some European populations have relatively high frequency of alleles with a deletion in gene for CCR5 receptor (CCR5-Δ32 allele). This allele offers some protection to HIV infection. CCR5-Δ32 allele is thought to have originated long prior to the HIV epidemic (1000-1200 years ago?). Instead, it may have risen to moderately high frequency due to protection it confers from some other disease (smallpox?).



"The modern-day observed allele frequencies [of CCR5-Δ32 allele]. Squares mark locations of sampled allele frequencies, and color within the squares denotes the observed frequencies. Contour lines represent interpolated allele frequencies."

Quote and Figure 1B from Galvani and Novembre. 2005. Microbes and Infection 7(2): 302-309.

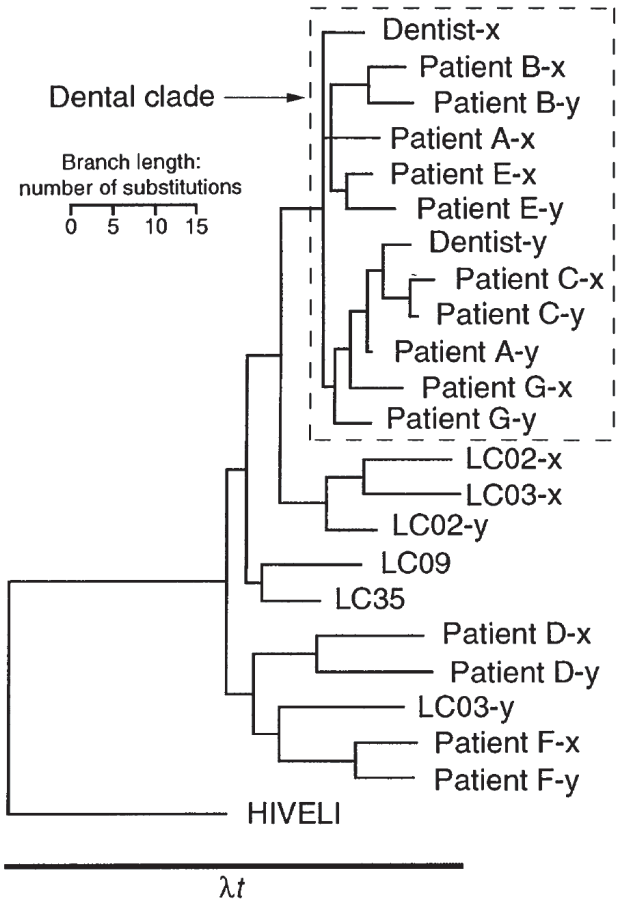


Fig. 3. Estimated phylogeny of HIV sequences from a Florida dentist, seven of his HIV-seropositive patients, and four individuals from the local population (LC) whose HIV sequences were most similar to those of the dentist (*47*). The outgroup (HIVELI) is an African HIV-1 sequence. Two divergent HIV sequences (labeled x and y) were examined from most individuals. The dental clade consists of patients whose HIV sequences are closer to those of the dentist than to those of any of the local controls. Branch lengths are proportional to the number of inferred evolutionary changes averaged across all possible character reconstructions (from *MacClade*) (*20*). The bar labeled λt is the distance from the root to the most divergent tip; it also indicates the divergence scale for the simulations in Fig. 4.

From Hillis et al. 1994. Science 264:671-677.

March 1998: Six medical workers (5 Bulgarian nurses, 1 Palestinian doctor) enter Libya to work at Al-Fateh hospital

Later in 1998: HIV (and Hepatitis C) outbreak discovered at Al-Fateh hospital. 438 children infected (at least 56 have now died). Medical workers accused of bioterrorism (i.e., intentionally spreading HIV).

2004: Medical workers sentenced to death by Libyan court

2006: Death sentence upheld following appeal
(December 2006 - Nature paper published)

2007: Medics pardoned, $438 million settlement?

5 Bulgarian nurses and 1 Palestinian doctor sentenced to death in Libya.

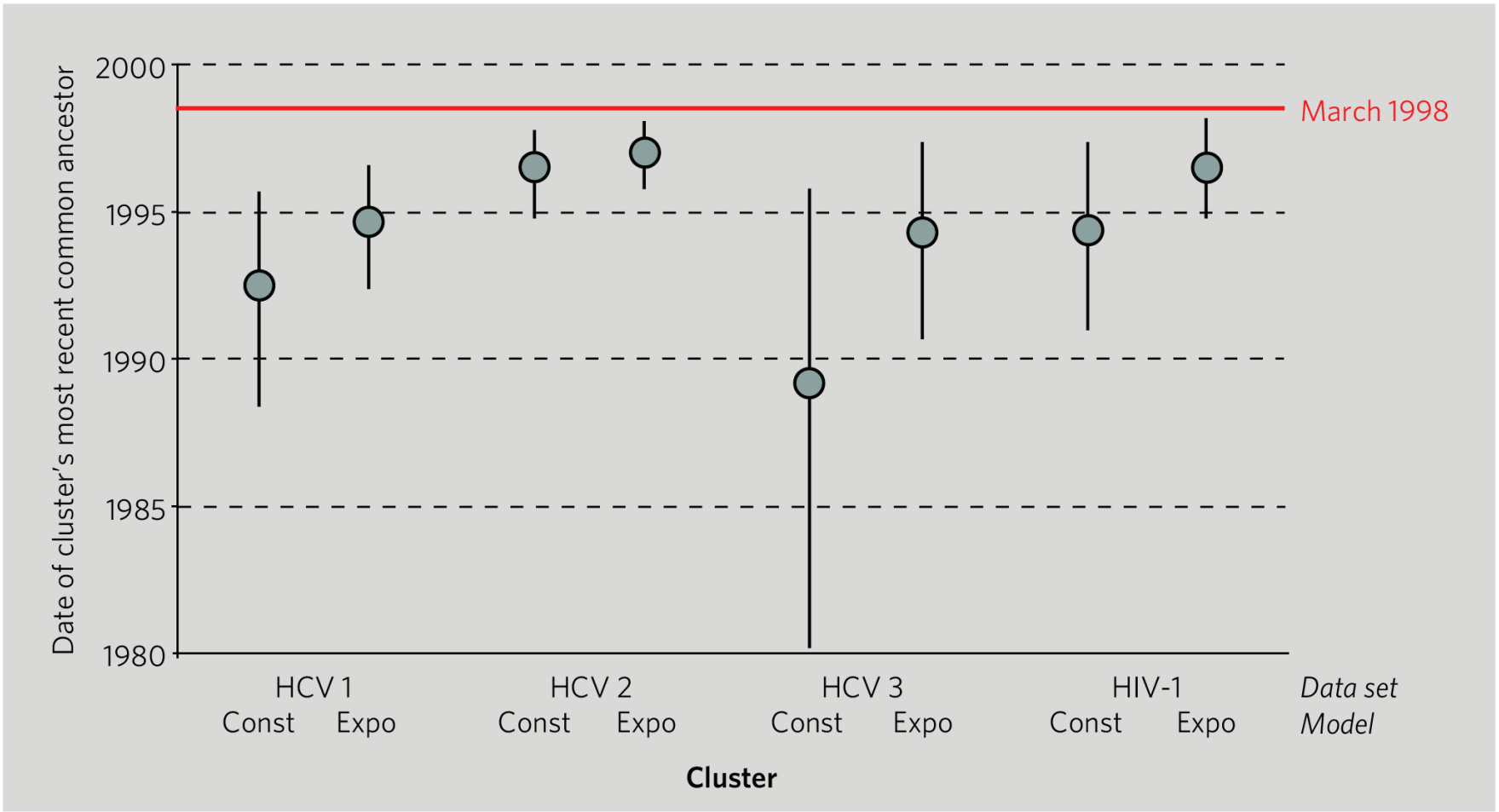


Figure 2 | Estimated dates of the most recent common ancestor for each cluster. Results obtained by using different evolutionary models. Vertical lines show the 95% highest posterior density intervals. Red line shows time of arrival of the foreign staff in March 1998. For further details, see supplementary information. 'Const', constant size; 'Expo', exponential growth.

Oliveira et al. Nature. published online 6 Dec. 2006.