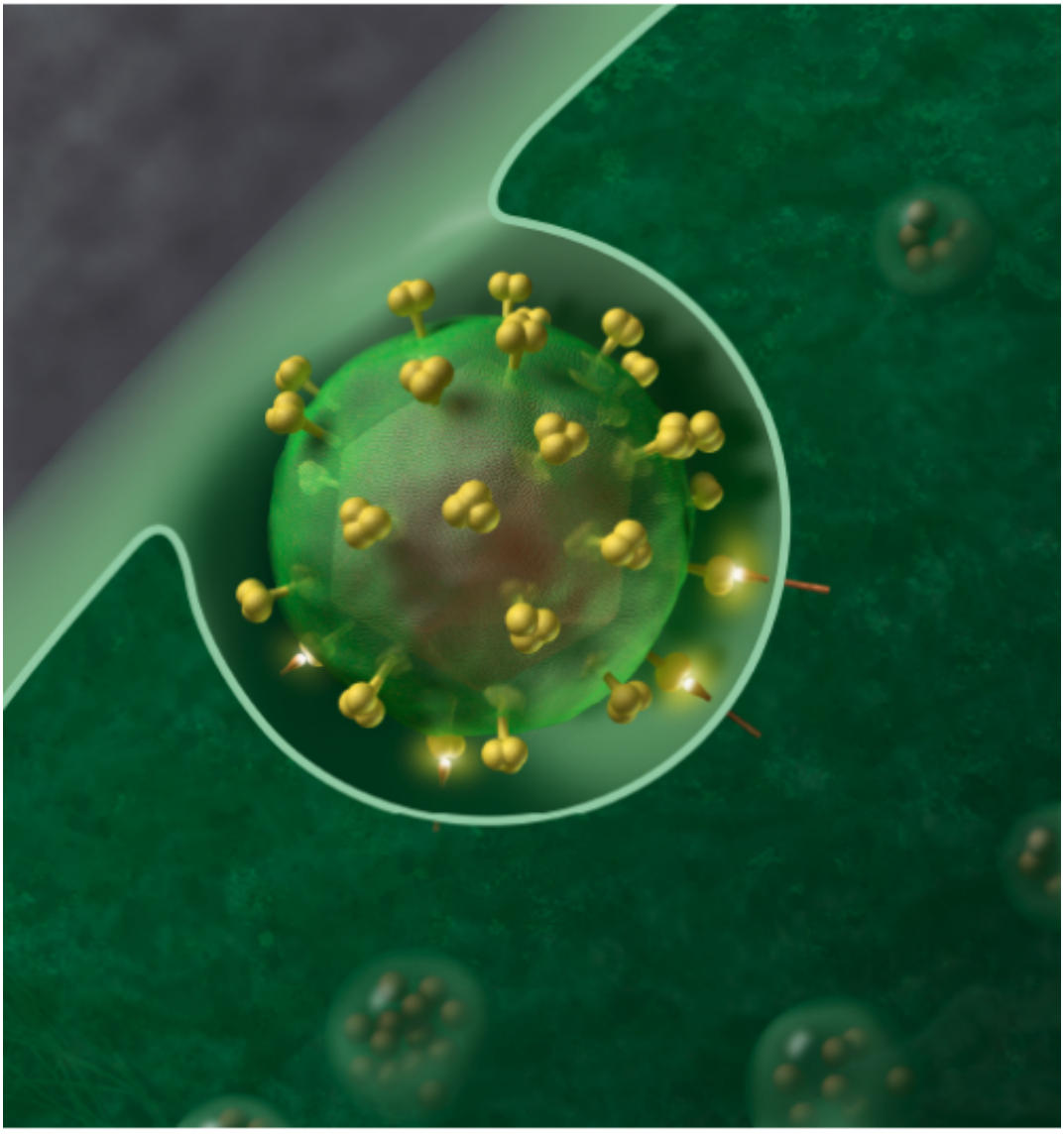
Research effort reveals gene variants that play a role in HIV viral load in patients

November 10 2015, by Bob Yirka



HIV-1 Virus. Credit: J Roberto Trujillo/Wikipedia

(Medical Xpress)—A large international team of researchers has conducted a study that has shed some light on the role genetic variation plays on HIV viral load levels in patients infected with the virus. In their paper published in *Proceedings of the National Academy of Sciences*, the team describes their study and results and what they believe needs to be done going forward.

HIV is, of course, the virus that leads to AIDS, and while at lot has been learned about it over the past several decades more work needs to be done to find a cure for it. In this new effort, the researchers sought to find the gene variants that are believed to be responsible in part for load level differences in people infected with the disease. The load level refers to the amount of HIV found in a given sample of blood once the disease has stabilized—lower levels are generally an indication that the immune system is putting up a strong fight, while high levels generally indicate the opposite. It is believed that load levels vary between individuals due to genetic, environmental and other factors.

To isolate the gene variants involved, the researchers obtained health information for 7,468 people of European decent who had participated in eight different HIV studies. Of those, 6,315 included data on viral load set points and thus were able to be used in the study. To find the variants, the team studied 8 million variants and in so doing uncovered what they believed to be two significant variants—one on chromosome 6, in the MHC region and the other on chromosome 3 in the CCR region.

Subsequent testing suggested that approximately 12.3 percent of viral set point variations could be attributed to the variant in the MHC region, and 2.2 percent to the CCR region, for a combined result total of 14.5 percent. They narrowed that percentage down further by taking into account genome-wide significant signals, leaving a 5 percent variation.

The team proposes similar studies be undertaken for non-European populations and for variant classes that have not been assessed by genome-wide association studies, to gain a more complete picture of the genetic factor in load points.

More information: P. J. McLaren et al. Polymorphisms of large effect explain the majority of the host genetic contribution to variation of HIV-1 virus load, *Proceedings of the National Academy of Sciences* (2015). DOI: 10.1073/pnas.1514867112

Abstract
Previous genome-wide association studies (GWAS) of HIV-1–infected populations have been underpowered to detect common variants with moderate impact on disease outcome and have not assessed the phenotypic variance explained by genome-wide additive effects. By combining the majority of available genome-wide genotyping data in HIV-infected populations, we tested for association between ∼8 million variants and viral load (HIV RNA copies per milliliter of plasma) in 6,315 individuals of European ancestry. The strongest signal of association was observed in the HLA class I region that was fully explained by independent effects mapping to five variable amino acid positions in the peptide binding grooves of the HLA-B and HLA-A proteins. We observed a second genome-wide significant association signal in the chemokine (C-C motif) receptor (CCR) gene cluster on chromosome 3. Conditional analysis showed that this signal could not be fully attributed to the known protective CCR5Δ32 allele and the risk P1 haplotype, suggesting further causal variants in this region. Heritability analysis demonstrated that common human genetic variation—mostly in the HLA and CCR5 regions—explains 25% of the variability in viral load. This study suggests that analyses in non-European populations and of variant classes not assessed by GWAS should be priorities for the field going forward.