ABSTRACT

Genetics of HIV-associated sensory neuropathy in black Southern Africans

Liesl Mary Hendry

HIV-associated sensory neuropathy (HIV-SN) is a common complication associated with human immunodeficiency virus (HIV)-infection. A common symptom of HIV-SN is pain. Variation at specific loci within certain candidate genes has been suggested to alter susceptibility to developing HIV-SN as well as the susceptibility to developing pain and the intensity of the pain experienced. Few studies, however, have been conducted in individuals of black African ancestry. The aim of the current research was to conduct an in-depth study, in a black Southern African population, of genes previously associated with susceptibility to developing HIV-SN (*TNFA* and surrounding genes and *IL12B*) and variations in pain susceptibility and intensity (*GCH1, KCNS1, IL1B, IL6, CCL2* and *CCR2*) in other neuropathic pain states. Single nucleotide polymorphisms (SNPs) identified in the literature were supplemented with population appropriate tagSNPs to improve assessment of the genes in an African population. Genotyping of previously collected deoxyribonucleic acid (DNA) samples was carried out using a GoldenGate assay with VeraCode microbeads and data were read on an Illumina BeadXpress Reader. Data were statistically analysed to assess the association of the genetic variants with susceptibility to developing HIV-SN and pain and variability of pain intensity in those patients with painful HIV-SN. Although some SNPs and haplotypes in the genes investigated associated with HIV-SN susceptibility (*TNFA* region), pain susceptibility (*TNFA* region, *IL12B, KCNS1, IL6* and *CCR2*) or pain intensity (*TNFA* region, *KCNS1, IL1B* and *IL6*), none of the results were consistent with that which has been found in previous studies in non-African populations. Reasons for this may be that associations are population-specific or model-specific. Limitations of the study included the

use of a relatively small sample, the method of sampling (convenience sampling), genotyping failure and tagging inefficiency in some instances, and the fact that there is no Southern African population dataset to use for tagSNP selection. My findings emphasise the importance of conducting genetic association studies in separate ethnic groups.