Prostate cancer has become the second leading cancer among men across ethnic groups in the world. Since it is influenced by a complex genetics that may affect the level of susceptibility for the development of the disease, four Y-linked short tandem repeats (STRs), DYS388, DYS435, DYS437, and DYS439 were genotyped to compare Malaysian prostate cancer patients and normal controls males. A total of 175 subjects comprising 84 patients and 91 healthy individuals from three major ethnics were recruited. Multiplex PCR was optimized to co-amplify all four DYS loci. All samples were genotyped for alleles of four DYS loci using a Genetic Analysis System. Result showed that allele 10 (A) of DYS388 had a significantly lower incidence towards disease than other alleles of this locus, while allele 12 (C) of DYS388 and allele 14 (E) of DYS439 showed a significantly higher risk to develop prostate cancer compared to other alleles of these loci. Moreover, among 47 different haplotypes comprising different alleles of four DYS loci found in the overall study samples, it is noticed that AABC and CAAA showed a lower and higher frequency among cases than controls, respectively. As a conclusion, Malaysian males who belong to Y-lineages with either allele 12 of DYS388, allele 14 of DYS439, or haplotype CAAA tend to develop prostate cancer. Meanwhile, those belonging to Y-lineages with allele 10 of DYS388 or haplotype AABC are more resistant to the disease. Thus, it is suggested that genetic elements give an influence on the development of prostate cancer.