Genetic Polymorphisms in SLCO1B3 and SLCO2B1 May Influence the Racial Difference in the Response to Androgen Deprivation Therapy in Advanced Prostate Cancer

Introduction and Objective: Japanese patients experience better cause-specific and overall survivals after androgen deprivation therapy (ADT) initiation compared with Caucasians. The underlying mechanisms of these ethnic differences are little understood. SLCOs encode organic anion transporting polypeptides (OATPs) that transport a variety of exogenous and endogenous substances including androgens. *SLCO1B3* and *SLCO2B1* are polymorphic, and single nucleotide polymorphisms (SNPs) alter transport efficiency of androgen. In the present study, we investigated association between SNPs in *SLCO1B3* and *SLCO2B1* and response to ADT and compared genotype frequencies of those genes between Japanese and Caucasians.
Materials and Methods: A cohort of 252 Japanese men, 152 with prostate cancer and 100 without prostate cancer, were genotyped for *SLCO1B3* (rs4149117) and *SLCO 2B1* (rs12422149). Genotypes were confirmed by sequencing of genomic DNA extracted from blood cells. In 72 men treated with primary ADT for advanced prostate cancer, association between SNPs in *SLCO1B3* and *SLCO2B1* and time to progression (TTP) during ADT was examined.
Results: *SLCO1B3* and *SLCO2B1* alone did not influence TTP during ADT. However, patients carrying both active androgen transport *SLCO1B3 (TT/TG)* and *SLCO2B1 (GG)* polymorphisms exhibited a median TTP of 7.5 months shorter than patients with impaired androgen-transporting activity *SLCO1B3* (GG) and *SLCO2B1(AG/AA)* polymorphisms (19.0 vs 11.5 months, $p = 0.003$). Men with combined impaired androgen transport genotypes comprised 30.2% (76/252), while men with combined elevated androgen transport genotypes comprised 19% (48/252). These frequencies were significantly more and less, respectively, compared with reported data in Caucasians.
Conclusions: Our results suggest that difference in genotype frequencies of *SLCO1B3* and *SLCO2B1* may be associated with racial differences in response to ADT.