IFNL3/4 polymorphisms are associated with AIDS-related Kaposi's sarcoma

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BACKGROUND
Kaposi's sarcoma (KS), the most common AIDS related cancer, represents a major public concern in resource-limited countries. Single nucleotide polymorphisms within the Interferon lambda 3/4 region (IFNL3/4) determine the expression, function of IFNL4, and influence the clinical course of an increasing number of viral infections.

OBJECTIVES
To analyze whether IFNL3/4 variants are associated with susceptibility to AIDS-related KS among men who have sex with men (MSM) enrolled in the Swiss HIV Cohort Study (SHCS).

METHODS
The risk of developing KS according to the carriage of IFNL3/4 SNPs rs8099917 and rs12980275 and their haplotypic combinations was assessed by using cumulative incidence curves and Cox regression models, accounting for relevant co-variables.

RESULTS
KS was diagnosed in 221 of 2558 MSM Caucasian SHCS participants. Both rs12980275 and rs8099917 were associated with an increased risk of KS (cumulative incidence 15% versus 10%, P = 0.01 and 16% versus 10%, P = 0.009 respectively). Dihptotypes predicted to produce the active P70 form (cumulative incidence 16% versus 10%, P = 0.01) but not the less active S70 (cumulative incidence 11% versus 10%, P = 0.7) form of IFNL4 were associated with an increased risk of KS, compared to those predicted not to produce IFNL4. The associations remained significant in a multivariate Cox regression model after adjustment for age at infection, combination antiretroviral therapy, median CD4 T-cell count nadir and CD4 slopes (HR = 1.43, 95% confidence interval 1.06-1.93, P = 0.02 for IFNL P70 versus no IFNL4).
CONCLUSION
This study reports for the first time an association between IFNL3/4 polymorphisms and susceptibility to AIDS-related KS.

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