Natural killer cell cytotoxicity is influenced by QPY/RAH haplotypes of the \textit{GZMB} gene.

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Natural killer (NK) cells constitute approximately 10\% of the lymphocytes in human peripheral blood. Granzyme B (GzmB) is a component of cytolytic granules within NK cells and is involved in several pathologies. In the presence of perforin, GzmB escapes from the endolysosomal compartment and gains access to a number of important proteins involved in the execution of the apoptotic program. It has previously been reported that there are three non-synonymous coding SNPs (rs8192917; Q48R, rs11539752; P88A, and rs2236338; Y245H) in the \textit{GZMB} gene, and that the QPY/RAH allele was clustered together close to the C-terminal $\alpha$-helix. However, it is unknown whether the function of GzmB produced from NK cells is influenced by QPY/RAH polymorphism. The authors investigated the distribution of QPY/RAH polymorphism of the \textit{GZMB} gene in a Japanese population (n = 106), and the involvement of Q48R polymorphism in NK cell cytotoxicity, degranulation, and production of GzmB. A strong linkage disequilibrium was observed among these SNPs, and NK cell cytotoxicity was influenced by rs8192917 (Q48R). Moreover, it found that R\textsuperscript{48}-GzmB is a stable protein that accumulates to similar levels in activated NK cells as Q\textsuperscript{48}-GzmB. The rs8192917 polymorphism may influence antitumor activity and the effect of antitumor cellular immunotherapy. Our study helps to provide a clearer understanding of the linkage disequilibrium among coding SNPs of the \textit{GZMB} gene. The authors expect that these new informations about QPY/RAH polymorphism of the \textit{GZMB} gene could help to assess the impact of NK cell cytotoxicity in several pathologies and aid their treatment.