IMMUNOTHERAPY

Predicting HSCT outcome in patients with neuroblastoma

New evidence from Jeffrey Venstrom and colleagues suggests that a lack of one or more human leukocyte antigen (HLA) ligands for killer immunoglobulin-like receptors (KIRs)—resulting in altered natural killer cell function—is associated with an increased survival rate in individuals with high-risk neuroblastoma undergoing hematopoietic stem cell transplantation (HSCT). “We had previously noted that certain gene combinations linked to natural killer cell function were predictive of improved outcomes for patients with acute myelogenous leukemia undergoing blood stem cell transplantation” explains lead investigator Katharine Hsu, “and we wished to determine if these same combinations would predict improved outcomes for patients with a solid tumor who undergo HSCT.”

The researchers genotyped 169 patients with stage IV neuroblastoma who had recently undergone HSCT and detected a lack of one or more HLA ligands for

inhibitory KIR in 64% of participants—individuals they refer to as having a ‘missing ligand’ KIR–HLA compound genotype. All patients had comparable tumor aggression regardless of whether or not they had a full KIR–HLA ligand complement.

Hsu’s team noted that patients lacking a HLA ligand had a 46% lower risk of death and a 34% lower risk of disease progression at 3 years follow-up when compared with individuals possessing a full KIR–HLA ligand complement. Following univariate and multivariate analysis, the investigators found that the ‘missing ligand’ genotype was significantly associated with survival compared with other known prognostic variables. Furthermore, 16 patients lacking the HLA ligand for KIR2DL2/KIR2DL3 receptors had the highest survival rate in comparison with participants lacking HLA ligand groups for other KIRs (KIR2DL1 and 12KIR3DL1).

The investigators stress that KIR–HLA immunogenetics may be useful as an additional prognostic biomarker to identify patients with high-risk neuroblastoma who are more likely to benefit from HSCT. “Individuals with specific KIR–HLA gene combinations may have an increased ability to clear their tumor, at least after autologous HSCT” concludes Hsu. The researchers next plan to investigate if HSCT is a necessary condition to harness the predictive effects of these specific KIR–HLA gene profile combinations or whether patients with neuroblastoma who do not receive HSCT still benefit from the alterations in natural killer cell activity.

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Original article Venstrom, J. M. *et al.* KIR and HLA genotypes are associated with disease progression and survival following autologous hematopoietic stem cell transplantation for high-risk neuroblastoma. *Clin. Cancer Res.* **15**, 7330–7334 (2009)