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Killer cell immunoglobulin-like receptor and HLA ligand pairs: A role in NK cell licensing in HLA class I mismatched hematopoietic stem cell transplantation for malignancy

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NK cell licensing effect highly increases the NK cell reactivity against tumor and is dependent on the co-expression of inhibitory killer cell immunoglobulin-like receptor (iKIR) and its cognate HLA class I ligand. In NK cell licensing cognate, KIR-HLA pairs are crucial. We assessed tumor outcomes (progression free survival-PFS and relapse incidence-RI) in 283 patients including strata with deficient NK cell licensing due to HLA class I mismatch. Patients underwent HSCT from unrelated donors due to myelo- or lymphoproliferative malignancies. We found dramatically reduced PFS (52.3% to 8.4%, $P=0.00010$) and increased RI (17.3% to 30.0%, $P=0.013$) among patients with the licensing downward resetting status after transplantation from HLA mismatched donor. The extremely adverse PFS have withstood the correction when stratified groups were restricted to HLA mismatched donor-recipient pairs (52.0% vs. 8.4%, $P=0.00087$). Among patients without the licensing downward resetting status after transplantation from HLA mismatched donor, the PFS and RI were similar to patients transplanted from fully matched donors. The incidence of a GvHD was comparable in licensed and downward resetting groups of patients. We conclude that anti-tumor function of repopulated donor NK cells is associated with iKIR-HLA-dependent licensing and it can be lost in malignant patients after HSCT if the mismatched HLA ligand in patient does no longer belong to cognate iKIR-HLA pair. The therapeutic effect of NK cell-based tumor immunotherapy is highly dependent on the sustained NK cell licensing.

Biography

Jacek Nowak has completed his PhD from Military Medical Academy and Postdoctoral studies from Institute of Hematology and Transfusion Medicine, Warsaw, Poland where he is the Associate Professor and Head of the Department of Immunogenetics. He has published more than 55 papers in reputed journals and 21 chapters and has been serving as an Editor of three international and domestic books.

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