Immunotherapy for EBV-associated Disorders

Wenwei Tu

Department of Paediatrics & Adolescent Medicine, LKS Faculty of Medicine, The University of Hong Kong. Hong Kong

Immunotherapy is a therapeutic strategy by regulating the patients' immune function to treat diseases, i.e. enhancing the immune responses to fight cancer; inhibiting the immunity to control autoimmune diseases or induce immune tolerance, etc. Here, we share our own research experience by regulating host Vγ9Vδ2-T cell function to treat EBV-associated disorders using EBV-induced lymphoproliferative disease (EBV-LPD) as a model. We showed that the aminobisphosphonate pamidronate-expanded human Vγ9Vδ2-T cells efficiently killed EBV-transformed autologous lymphoblastoid B cell lines (EBV-LCL) through γ/δ-TCR and NKG2D receptor triggering, and Fas and TRAIL engagement. By inoculation of EBV-LCL in $Rag2^{-/-}\gamma c^{-/-}$ mice and humanized mice, we established lethal EBV-LPD with characteristics close to the human disease. Adoptive transfer of pamidronate-expanded Vγ9Vδ2-T cells alone effectively prevented EBV-LPD in $Rag2^{-/-}\gamma c^{-/-}$ mice and induced EBV-LPD regression in EBV^{+} tumor-bearing $Rag2^{-/-}\gamma c^{-/-}$ mice. Pamidronate treatment inhibited EBV-LPD development in humanized mice through selective activation and expansion of Vγ9Vδ2-T cells. This study provides proof-of-principle for a novel therapeutic approach using pamidronate to control EBV-LPD through Vγ9Vδ2-T-cell targeting. As pamidronate has been already used for decades in osteoporosis treatment, this 'new application of an old drug' potentially offers a safe and readily available option for the treatment of EBV-LPD.