

Plasma EBV microRNAs in paediatric renal transplant recipients

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- **Abstract**

Background: Epstein-Barr virus (EBV) was the first human virus identified to express microRNA (miRNA). To date, 44 mature miRNAs are encoded for within the EBV genome. EBV miRNAs have not been profiled in paediatric renal transplant recipients. In this study, we investigated circulating EBV miRNA profiles as novel biomarkers in paediatric renal transplant patients.

Methods: Forty-two microRNAs encoded within 2 EBV open reading frames (BART and BHRF) were examined in renal transplant recipients who resolved EBV infection (REI) or maintained chronic high viral loads (CHL), and in non-transplant patients with acute infectious mononucleosis (IM).

Results: Plasma EBV-miR-BART2-5p was present in higher numbers of IM (7/8) and CHL (7/10) compared to REI (7/12) patients. A trend was observed between the numbers of plasma EBV miRNAs expressed and EBV viral load ($p < 0.07$). Several EBV-miRs including BART7-3p, 15, 9-3p, 11-3p, 1-3p and 3-3p were detected in IM and CHL patients only. The lytic EBV-miRs, BHRF1-2-3p and 1-1, indicating active viral replication, were detected in IM patients only. One CHL patient developed post-transplant lymphoproliferative disease (PTLD) after several years and analysis of 10 samples over a 30-month period showed an average 24-fold higher change in plasma EBV-miR-BART2-5p compared to the CHL group and 110-fold higher change compared to the REI group.

Conclusions: Our results suggest that EBV-miR-BART2-5p, which targets the stress-induced immune ligand MICB to escape recognition and elimination by NK cells, may have a role in sustaining high EBV viral loads in CHL paediatric kidney transplant recipients.

Keywords: EBV miRNA; EBV viral load; Plasma EBV-miR-BART2-5p; Renal transplant recipients.