

[BIO14]

Genotypic and functional comparison of *Epstein-barr* virus latent membrane protein-1 from different stages of nasopharyngeal carcinoma

Tan Eng Lai, Sam Choon Kook

NPC Laboratory, C503, Institute of Postgraduate Studies, University of Malaya, 50603 Kuala Lumpur.
E-mail: englai@eudoramail.com

A preliminary survey of the prevalent LMP1 genotypes in Malaysian NPC was conducted. Analyses of LMP1 genotypes from 49 positive throat wash samples from patients with NPC showed high incidence of the loss of *Xho*I restriction site at exon A (81%) and 30-bp deletion at exon C (20%). While, none of the throat washes from healthy controls exhibited the *Xho*I polymorphism, the 30-bp deletion was detected in 8% of the healthy PNS biopsies. LMP1 genes derived from two histological stages of NPC were investigated. LMP1 cDNAs were cloned from a pre-malignant (NORLMP1) and a malignant lesion (NPCLMP1) and their DNA sequences, antigenicity and biological properties were evaluated and compared to the wild-type B95LMP1 and AGLMP1 cDNAs cloned, respectively, from B95.8 and AG876 cell lines. DNA sequencing of NORLMP1 and NPCLMP1 revealed two histological stage-specific LMP1 variants that shared both the 30-bp deletion and *Xho*I polymorphism but were largely heterologous where point and insertional mutations were concerned. Base insertions in NPCLMP1 rendered it an additional unit of internal repeat. These mutations collectively resulted in NORLMP1 and NPCLMP1 that were, respectively, 371 and 382 amino acid residues in length. NORLMP1 and NPCLMP1 expressed in yeast displayed different antigenicity and demonstrated diverse biological properties when transfected into the EBV-negative NPC cell line, TW01. They differed in terms of their abilities to down-regulate E-cadherin expression. Both NORLMP1 and NPCLMP1-transfected TW01 cells were able to form tumours in athymic nude mice. Gene array-based analyses of cancer gene expression indicated that NORLMP1 and NPCLMP1 had dissimilar regulatory effects both *in vitro* and *in vivo*.