ARI-04

FUNCTIONAL ASSAYS OF HLA A2-RESTRICTED EPITOPE VARIANT OF LATENT MEMBRANE PROTEIN 1 (LMP-1) OF EPSTEIN-BARR VIRUS IN NASOPHARYNGEAL CARCINOMA IN SOUTHERN CHINA AND TAIWAN

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BACKGROUND: HLA A2 was consistently associated with increased risk for nasopharyngeal carcinoma (NPC) in Chinese populations.

METHODS and RESULTS: Functional assays of the epitope variant were carried out in the present work. The stabilization assay on T2 cells indicated that the variant peptide YFL (YFLEILWRL) prevalent in NPC binds to HLA-A2 molecules less efficiently than the prototype peptide YLL (YLLEMLWRL). A dose-dependent binding of the HLA-A2 molecules with added peptides was observed. Ex vivo cytotoxic T lymphocyte (CTL) assays with CD8-enriched effectors from A2-positive donors revealed that the YLL-specific CTL was able to lyse EBV-infected B cells expressing HLA-A2, whereas the CTL recognition was abrogated with the peptide YFL. Cytokine (IFN-γ) responses, measured both by intracytoplasmic staining and ELISPOT assays after peptide stimulation, also indicated that the variant epitope peptide failed to give an IFN-γ response. The IFN-γ response was almost entirely restricted to those tetramer-positive cells.

CONCLUSIONS: These results show that EBV isolates from NPC in southern China and Taiwan are dominated by HLA A2-restricted “epitope-loss variants” of LMP-1, which would allow the virus to resist immune recognition and may in part contribute to the prevalence of NPC in these populations.

Key words: Nasopharyngeal carcinoma, LMP-1 oncoprotein, EBV, A2-restricted epitopes, cytotoxic T lymphocytes, functional domains