00549 Translating LMP2A as a Bonafide Cancer Target After Bioinformatic Assessment of Cross-strained Homology

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Aims: Epstein-Barr virus (EBV) related cancers are prevalent in Asia and lack immune diagnostic studies and immunotherapy. Thus, this study plans to discover EBV-specific immune epitopes as potential targets for cancer immunotherapy. To develop a therapeutic strategy for a broad spectrum of these cancers, the target sequences must be highly conserved between strains. Due to the extracellular accessibility of surface proteins, latent membrane proteins (LMP) LMP1, LMP2A and LMP2B of EBV were identified as potential epitopes.

Methodology: The entire genome of 97 strains was obtained from public databases. Percentage identity tests were performed between the EBV B95-8 reference strain, NC-007065, and the other 96 strains for all LMPs. A Matlab script extracted the conserved sequences coding for extracellular regions for each LMP throughout all strains.

Result: Percentage identity tests showed that LMP2A and LMP2B are highly homogeneous, with each strain being at least 97% similar to NC-007065 while LMP1 only assured a similarity of at least 76%. LMP2A and LMP2B are consistent in their lengths of 497 and 378 amino acids respectively across all strains but LMP1 is not. Following UniProt's topology of NC-007065's LMPs, the positions coding for extracellular regions can be identified. However, UniProt has only the topology of LMP2A and LMP1.

Between both, as only LMP2A maintains a constant length, assuming that the positions coding for the extracellular regions as annotated for NC-007065 is the same across strains, the sequences can be identified for all strains. Two possible extracellular target regions of 55 amino acids for LMP2A were identified, one conserved in 65 strains and the other, in 61. As a follow-up, we attempted expressing LMPs from NC-007065 in eukaryotic cells and demonstrated expression of these proteins with western blot and immunohistochemistry.

Conclusion: LMPs are promising target proteins in EBV related cancers due to the high conservation across various EBV strains.